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GONIOLITHON AND NEOGONIOLITHON: TWO GENERA OF CRUSTACEOUS CORALLINE ALGAE

By William Albert Setchell and Lucile Roush Mason

Department of Botany, University of California

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Foslie, in his earlier studies of the crustaceous Corallines, proposed a new genus *Goniolithon* (see Foslie, "Syst. Surv. Lithoth.," 5 (1898), with scant description. He also described two subgenera, *Eugoniolithon*, apparently from his designation, the typical subgenus, and *Cladolithon*, the latter subgenus to include the fruticulose species. The type and only species of Eugoniolithon was the *Lithothamnion papillosum* Zanardini (as described by Hauck). This certainly is to be considered as the type of the genus *Goniolithon* of 1898. The only species referred to the subgenus *Cladolithon*, which in a footnote Foslie describes as a doubtful subgenus, is the *Lithophyllum byssoides* (Lam'k) Foslie, at that time a heterogeneous mixture in the mind of Foslie; as will be indicated later. Taking *G. papillosum* (Zan.) Foslie as the type of *Goniolithon*, the genus is a perfectly distinct entity, being made up of strictly monostromatic layers (without cover cells or perithallus of any kind) and belongs therefore to the subfamily *Mastophoreae* of the *Corallinaceae Crustaceae*, all of whose members have monostromatic (at times symmetrically di-polystromatic?) sterile frond structure, thus differing from all other Corallinaceae. The sterile fronds also have a way of obliquely and lamellately proliferating, and these proliferations produce superposed and distinct layers in *Litholepis* and *Lithoporella*, but are agglutinated into a solid frond in the original *Goniolithon*.

Later, in 1898 ("List of Species of the Lithoth.," p. 8) Foslie changes the name of the subgenus I. *Eugoniolithon* to subgenus I. *Lepidomorphum*, listing 4 species of which *G. papillosum* is first mentioned, while under subgenus II. *Cladolithon* he mentions *G. byssoides* first of 18 species and *G. moluccense* second. In 1900, in his "Revised Systematical Survey of the Melobesieae" (p. 15), Foslie rejects his earlier *Goniolithon* (of 1898) and proposes an entirely new *Goniolithon* distinguished by having the tetrasporangia distributed over the floor of the conceptacle and (incidentally

because he makes no mention of their occurrence) with heterocysts scattered through the perithallus. This new *Goniolithon* may be considered to have been founded on the *Lithothamnium moluccense* Foslie, since Foslie stated that his *G. byssoides* of 1898 was intended to refer to his *G. moluccense*. At any rate, Foslie has proposed two distinct genera under *Goniolithon*, the original in 1898 with the type *G. papillosum* (Zan.) Foslie and the other partly visualized under the doubtful subgenus *Cladolithon* in 1898 but only distinctly segregated about 1904 ("Siboga Exp.," Mon. LXI, 45 (1904)) and finally properly delimited (by the exclusion of *Hydrolithon*) in 1909 ("Algol. Notis.," VI).

Two facts stand out clearly: (1) that Foslie completely rejected his *Goniolithon* of early 1898; and (2) that Foslie gradually evolved a new *Goniolithon*, finally brought to full expression in 1909. The two genera are complete and fairly independent establishments, and no single species of *Goniolithon* No. 1 survived into *Goniolithon* No. 2. This condition might have been stabilized by an international botanical congress without change of name, were it not for the fact that the type of *Goniolithon* No. 1 (*Goniolithon papillosum*) is a generic type of its own, distinct not only from *Goniolithon* No. 2 but from all other genera. The proposal which seems most logical is to recognize *Goniolithon* No. 1, with type species *G. papillosum*, and to rename *Goniolithon* No. 2, *Neogoniolithon nov. nom.*, with such a species as is most characteristic and well described, as *G. Fosliei* (Heydr.) Foslie, for the type. The consequent changes are enumerated in the following paragraphs.

Goniolithon Foslie (restr. to subfamily *Mastophoreae*)

Fronds crustaceous to decidedly thick, composed of separate monostromatic layers arising from those immediately below by obliquely lamelliform proliferation and becoming cemented together; conceptacles simple (without thickening of frond tissue) in all types, opening by a simple pore.

Foslie, "Systematical Survey of the Lithothamnia," 5 (1898), as to subgenus I. Eugoniolithon (non aliorum, p.p. exceptorum). (!) means that the type specimen has been examined by, at least, one of us (Setchell).

Goniolithon papillosum (Zan.) Foslie (type!)

Lithophyllum papillosum Zanardini, "Saggio," 43 (1843) (!) (*sine descr.*) Hauck, "Meeresalgen, 272, pl. 2, fig. 4 (1885) (!). *Lithophyllum papillosum* Foslie *in* "Siboga Exp.," Mem. 61: 63, fig. 23 (*optime!*) (1904); *Melobesia Cystosirae* Hauck., loc. cit., 266, pl. 3, figs. 1, 2, 6 (1885); Adriatic Sea.

Goniolithon alternans (Lemoine) comb. nov.

Lithophyllum alternans Lemoine, *Archiv. Mus. Paris*, **4**: 64–66, figs. 22, 23, pl. fig. 3, pl. 3, fig. 9 (1929) (!); Galapagos Islands.

Goniolithon geometricum (Lemoine) comb. nov.

Lithophyllum (*Dermatolithon*) *geometricum* Lemoine *in* Boergesen, "Rhodophyc. Canary Islands," 17, fig. 17, pl. 1, fig. 4 (1929); Canary Islands.

Goniolithon preprototypum (Lemoine) comb. nov.

Lithophyllum preprototypum Lemoine, "Contrib. Etud. Corallin. fossil.," No. 3: 265, fig. 12 (1917); fossil on Ile de Martinique, W. I.

Goniolithon prototypum (Foslie) comb. nov.

Lithophyllum prototypum Foslie, "On Some Lithoth.," 18 (1897); Island of Santa Cruz, W. I. Possibly same as *G. Udoteae* Foslie (according to Lemoine).

Goniolithon tessellatum (Lemoine) comb. nov.

Lithophyllum (*Dermatolithon*) *tessellatum* Lemoine, *Archiv. Mus. Paris* **4:** 68–70, figs. 26, 27, pl. 1, figs. 3, 6, pl. 4, fig. 7 (1929) (!); Galapagos Islands.

Goniolithon Udoteae Foslie

Foslie, "New Melobesieae," 21 (1901); Island of Santa Cruz, W. I., see also *G. prototypum* (Foslie).

Goniolithon lapidea (Foslie) comb. nov.

Mastophora (*Lithostrata*) *lapidea* Foslie, "Algol. Notis.," II, 27 (1906); *Lithoporella lapidea* (Foslie) Foslie, "Syst. Bemerk," 59 (1909); Caspian Sea.

Species of *Goniolithon* (*verum!*) are frequent in elevated limestones, probably of the early Eocene period, in the Lau Islands between Fiji and Tonga in the Pacific Ocean. Studies are still in progress.

Neogoniolithon nom. nov.

Fronds from crustaceous to decidedly fruticulose and branched; hypothallus (basal or medullary) coaxial; perithallus of erect filaments, arising from the hypothallus; epithallus more or less distinct of flattened cells; heterocysts frequent or sparse, typically in short vertical rows; conceptacles of all three types, opening by a single pore; tetrasporangia uniformly (always?) distributed over the floor of the tetrasporangial conceptacle. Type species, *Lithothamnium Fosliei* Heydrich, *Ber. deutsch. bot. Gesell.*, **15,** 1897, p. 58, for the crustaceous species and *Goniolithon frutescens* Foslie, "Calcareous algae from Funafuti," 9 (1900), for the fruticulose or branched species. A considerable and widely distributed genus.

The following large number of incompletely known series of forms seem properly to be referred here.

Species Crustaceae

Neogoniolithon accretum (Foslie et Howe) comb. nov.

Goniolithon accretum Foslie et Howe, "New American Corall. Algae," 131, pl. 85, fig. 2, pl. 91 (1906); Bahama Islands, W. I. (!).

Neogoniolithon Fosliei (Heydrich) comb. nov.

Lithothamnium Fosliei Heydrich, *Ber. deutsch. bot. Gesell.*, **15,** 1897, 58 (p.p.), 410; Maldive and Laccadive Archipelagoes (!).

Neogoniolithon Hariotii (Foslie) comb. nov.

Goniolithon Hariotii Foslie, "Algol. Notis.," III, 13 (1907); Mangareva, in the Marquesas Archipelago (!).

Neogoniolithon megalocystum (Foslie) comb. nov.

Goniolithon megalocystum Foslie, "Siboga Exp.," Mon. 61: 48, fig. 20, pl. 9, figs. 8, 9 (1904); East Indies.

Neogoniolithon misakiense (Foslie) comb. nov.

Goniolithon misakiense Foslie, "New Lithoth.," 4 (1905); E. Japan.

Neogoniolithon myriocarpum (Foslie) comb. nov.

Lithothamnium myriocarpum Foslie, "On Some Lithoth.," 19 (1897); "*Goniolithon myriocarpon*" Foslie, "Siboga Exp.," Mon. 61: 45, pl. 9, figs. 6, 7 (1904); East Indies (!).

Neogoniolithon orthoblastum (Heydrich) comb. nov.

Lithothamnium orthoblastum Heydrich, *Ber. deutsch. bot. Gesell.*, **19:** 403 (1901). *Goniolithon orthoblastum* M. A. Howe, "Calc. Alg. fr. Murray Isl., Austral.," 291, pl. 97, fig. 2, pl. 98, figs. 1, 2 (1918); Papua (!).

Neogoniolithon pacificum (Foslie) comb. nov.

Goniolithon pacificum Foslie, "Nye Kalkalger," 6 (1908); E. Japan.

Neogoniolithon solubile (Foslie et Howe) comb. nov.

Goniolithon solubile Foslie et Howe, *in* Foslie, "Algol. Notis.," IV, 21 (1907); Island of Jamaica, W. I. (!).

Neogoniolithon versabile (Foslie) comb. nov.

Goniolithon versabile Foslie, "Algol. Notis.," III, 15 (1907); Japan.

Species Valde Verrucosae aut ramosae

Neogoniolithon affine (Foslie et Howe) comb. nov.

Goniolithon affine Foslie et Howe, *in* Foslie, "Algol. Notis.," IV, 22 (1907); Island of Culebra, W. I. *An Hydrolithon? aff. G. Boergesenii* Foslie?

Neogoniolithon assitum (Foslie) comb. nov.

Goniolithon assitum Foslie, "Algol. Notis.," IV, 23 (1907); Red Sea. (*An Hydrolithon? aut Porolithon?*)

Neogoniolithon brassica-florida (Harv.) comb. nov.

Melobesia brassica-florida Harvey, "Nereis Australis," 110 (1849); Algoa Bay, S. E. Africa.

Neogoniolithon finitimum (Foslie) comb. nov.

Goniolithon finitimum Foslie, "Nye Kalkalger," 8 (1908); S. E. Australia.

Neogoniolithon frutescens (Foslie) comb. nov.

Goniolithon frutescens Foslie, "Calc. Algae Funafuti," 9 (1900); "Siboga Exp.," Mon. 61: 53, 54, fig. 22, pl. 10, figs. 7–9 (1904); Indo-Pacific (!).

Neogoniolithon laccadivicum (Foslie) comb. nov.

Goniolithon laccadivicum Foslie, "Siboga Exp.," Mon. 61: 51, pl. 9, figs. 10–13 (1904); Indian Ocean (!).

Neogoniolithon mamillare (Harv.) comb. nov.

Melobesia mamillaris Harvey, "Nereis Australis," 109, pl. 41 (1849); Brazil.

Neogoniolithon mamillosum (Hauck.) comb. nov.

Lithothamnium mamillosum Hauck., "Meeresalgen," 23, pl. 3, fig. 3, pl. 5, fig. 1 (1885); Adriatic Sea.

Neogoniolithon Martellii (Sams.) comb. nov.

Goniolithon Martellii Sams., "Sopra due Alghe Calc. foss.," 241 (1914); Fossil, Albania.

Neogoniolithon Rhizophorae (Foslie et Howe) comb. nov.

Goniolithon Rhizophorae Foslie et Howe, "New Amer. Corall. Alg.," 130 (1906); Bahama Islands, W. I.

Neogoniolithon strictum (Foslie) comb. nov.

Goniolithon strictum Foslie, "New Melobes.," 14, (1901); M. A. Howe, *Jour. N. Y. Bot. Garden*, **6**, n. 64, with figure (1905); Florida and W. I. (!).

Neogoniolithon spectabile (Foslie) comb. nov.

Goniolithon spectabile Foslie, "New Melobes.," 16 (1901); Bermuda Islands. *G. strictum* Foslie et *G. intermedium* Foslie valde affine?

Neogoniolithon trichotomum (Heydrich) comb. nov.

Lithothamnium trichotomum Heydrich, "Lith. Mus. Paris," 538 (1901); Gulf of California. *G. frutescens* Foslie valde affine? (!)

The species transferred above seem reasonably to be referred to the second genus *Goniolithon* of Foslie, as renamed, of necessity, and by us, *Neogoniolithon*. Of the majority not mentioned here, renewed study of the type material is necessary to determine whether they are true Neogoniolithons or possibly to be referred to *Hydrolithon* or even to *Lithophyllum* or *Porolithon*.

NEW OR LITTLE KNOWN CRUSTACEOUS CORALLINES OF PACIFIC NORTH AMERICA

BY WILLIAM ALBERT SETCHELL AND LUCILE ROUSH MASON

DEPARTMENT OF BOTANY, UNIVERSITY OF CALIFORNIA

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Since 1895 and even from somewhat earlier, the senior author has been collecting and studying crustaceous Corallines, especially those from the Indo-Pacific area. Very early many of the specimens, particularly from the coasts of Pacific North America, were sent to M. Foslie at Trondhjem, Norway, the great authority on the groups, and were named and published upon by him. There exists, therefore, in the Herbarium of the University of California many duplicate types and other authentic material for the study of Pacific North American species as well as of adjacent areas.

The junior author prepared, as a Ph.D. thesis, a detailed account of the species of the coasts of Pacific North America, with illustrations, critical notes, as well as a general review of the subfamilies, of the genera, and species, ranging from Bering Straits to Panama. A copy of this thesis is deposited with the Library of the University of California, where it may be consulted.

The work has been continued by both authors and in the course of some years additional facts and modification of opinion have resulted. The following notes as to changes of nomenclature, of new species, and other such matters are detailed below.

1. **Lithothamnium giganteum** L. R. Mason sp. nov.

Frons crustacea, durissima, usque ad 6–8 mm. crassa, protuberantibus robustissimis, 10–15 mm. altis, 5–15 μ latis, apicibus quam basibus latioribus, munita, colore obscure cinerea, magnitudine 5 cm. 7 cm. et ultra; hypothallo tenue, ad superficiem totam lapillorum mediocrium non calcareorum, per superficem totam inferam, arcte adherente, 1–2 usque ad 80 cellulis crasso, cellulis 6–20 μ longis, 6–8 μ latis, elongatis cum substrato parallelis; perithallo 6–7 mm. crasso, crebre stratoso (stratis magnitudine formaque parvarum cellularum differentibus), cellulis isodiametricis, 5–6 μ diam., aut verticaliter leviterque elongatis 6–14 μ altis et 5–8 μ latis; epithallo 1–3 stratorum cellularum, cellulis horizontaliter applanatis, 2–4 μ alt., 5–7 μ lat.; conceptaculis tetrasporangiiferis 440–475 latis, 90–210 μ altis, poris 50–60 apertis; tetrasporangiis 4-divisis; conceptaculis spermatangiiferis cystocarpiiferisque nondum visis.

Spec. typ. La Jolla, California, No. 1514*a*; leg. N. L. Gardner.

This is by far the coarsest *Lithothamnium* on the Pacific coast of North America, as yet discovered. In habit and size, it superficially resembles *Lithothamnium crassiusculum* (Foslie) *comb. nov.* (see next species) but is more massive, thicker, harder and with more regularly arranged branchlets (or warts) swollen above and narrowed to a stalk-like base.

2. **Lithothamnium crassiusculum** (Foslie) L. R. Mason comb. nov.

Lithothamnium rugosum f. *crassiuscula* Foslie, "New Melobesieae," 4 (1900) (p.p.); *L. pacificum* f. *crassiuscula* Foslie, "Algol. Notis.," II, 10 (1906) (p.p.); Foslie, "Mon. Lithoth." (ed. H. Printz), 44, pl. 4, fig. 18 (1929).

Foslie based his "*crassiuscula*" on two specimens (Setchell 1149 and 1496*a*, the first from White's Point, near San Pedro, the second from San Pedro, California), referring it at first (1901) under *Lithothamnium rugosum* Foslie (1900), a Fuegian species, but later under *L. pacificum* Foslie (1906). Careful study both on the shore and on type material has convinced us not only of the independence of both *L. rugosum* and *L. pacificum* of one another but also of the fact that the f. *crassiuscula* included two different species, of which we refer No. 1149 Setchell to the proposed *Lithothamnium crassiusculum* and No. 1496*a* Setchell to an entirely new species, *Lithothamnium aculeiferum*, to be described below. The two species are very unlike both in habit and in structure. *L. crassiusculum* has coarse pro-

tuberances irregularly distributed but frequent, resembling superficially *L. giganteum* in habit, while *L. aculeiferum* has irregularly and sparsely distributed excrescences which are low and pointed.

3. **Lithothamnium aculeiferum** L. R. Mason sp. nov.

Frons crustacea, 1–3 mm. crassa ad saxa arcte per totam superficiem inferam adherente vulgo lapillos parvos ab undis circumjactis prorsus circumdata, colore vivo roseo-purpureo siccitate purpureo-cinereo, excrescentibus numerosis angularibusque, humilibus, 1–1.5 mm. alt., basi 1–2.5 mm. lat., vulgo ad apicem acutam attenuatis; hypothallo aut tenuiter evolvato aut passim usque ad 150–200 μ alt., cellulis elongatis, 10–30 μ long., 6–10 μ alt., parallelis, et in angulis rectis perithallum faciendum assurgentibus, perithallo 1–2.5 mm. crasso, saepe per differentiam parvam cellularum magnitudinis stratoso, cellulis isodiametricis, lente elongatis, aut ad superficiem superam paralleliter applanatis, ad angulos rotundatis, 5–8 μ lat., 3–9 μ alt.; epithallo 1–3 cellulo-stratos, cellulis 5–7 μ lat., 1–3 μ alt., applanatissimis, vulgo multo contusis; conceptaculis sporangiiferis convexis, 95–160 μ alt., vulgo ad superficiem superam parallelis leviter applanatis, poris 15–40, uniquibusque circum 20 μ diam.; tetrasporangiis 90–150 μ alt., 60–75 μ lat., transverse 2-divisis, conceptaculis cystocarpiiferis convexis, 425–500 μ diam.; conceptaculis spermatangiiferis nondum visis.

Lithothamnium rugosum f. *crassiuscula* Foslie, "New Melobesieae," 4 (1901) (p.p.); *L. pacificum* f. *crassiuscula* Foslie, "Algol. Notis.," II, 10 (1906) (p.p.).

The type specimen is No. 1496*a*, Setchell, collected near San Pedro, California, and especially that part of the collection preserved in the Herbarium of the University of California. It has also been collected at Pacific Grove, California (Maurice B. Nichols, Nos. 126, 181, in Herb. Univ. Calif.), and at La Jolla, California (Maurice B. Nichols, No. 382, in Herb. Univ. Calif.).

Foslie's description of his f. *crassiuscula* seems to have been drawn from Setchell No. 1149, which differs from Setchell No. 1496*a* in habit, structure, number of pores of the tetrasporangial conceptacle, and number of divisions in the tetrasporangium. The name, promoted to specific rank, is retained for, and restored to, No. 1149 and its like, while No. 1496*a* (and its like) has been made the type of *Lithothamnium aculeiferum*.

4. **Lithothamnium validum** Foslie *nom. delend.*

Foslie, "Algol. Notis.," II, 10 (1906); Setchell and Gardner, *Proc. Calif. Acad. Sci.*, ser. 4, **19**: 197 (1930); *Lithoth. rugosum* f. *valida* Foslie, "New Melobesieae," 4 (1900) (omnibus p.p.).

A study of a portion of the type material (Herb. Farlow, No. X, collected near San Diego, by H. Hemphill) indicates that this species of Foslie is a composite and therefore the binomial is to be rejected. The internal structure described is that of a *Lithothamnium* but the external structure is that of a *Lithophyllum*. The latter, later described by Foslie as *Lithophyllum imitans* ("Algol. Notis.," VI, 13 (1909)), is a species fairly readily recognized by its coarseness, covered by many short obtuse branchlets and the glossy (or glazed) surface of both the horizontal crust and the branchlets.

5. **Melobesia mediocris** (Foslie) comb. nov.

Lithophyllum mediocris Foslie, "Algol. Notis.," III, 33 (1906); *Lithophyllum zostericolum* f. *mediocris* Foslie, "Five New calcareous algae," 5 (1900); *Lithothamnium mediocris* Foslie et Nichols, *in* Nichols, *Univ. Calif. Pub. Bot.*, **3:** 341–348, pl. 9 (1908); *Melobesia amplexifrons* Farlow, *Proc. Amer. Acad.*, **12:** 239 (1877) (non Harv.).

Since *Melobesia*, as restricted in accordance with the type species, *M. membranacea* (Esper) Lamouroux ("Nouv. Bull. Sci.," p. 1. *Soc. Philomat.*, V, **3:** 186 (1812)) must take precedence of *Epilithon* Heydrich ("Melobesieae," 408 (1897)), it is necessary to make this new combination for our Californian plant. It, together with *Melobesia marginata* Setchell et Foslie represents the genus on our coasts.

6. **Lithophyllum neofarlowii** nom. nov.

Lithophyllum Farlowii Foslie, "New Melobesieae," 12 (Feb. 18, 1901) non L. Farlowii Heydrich, "Lithoth. Mus. Paris," *in* Engler's *Bot. Jahrb.*, **28:** 532, pl. 1, fig. 6 (Jan. 12, 1901).

The proposing of the name *Lithophyllum Farlowii*, at almost the same time, by Foslie for a Californian species and by Heydrich for a Galapagos species, was seemingly settled when Heydrich incorrectly assumed the priority of Foslie's name and rechristened the species from the Galapagos Islands *L. claudescens* Heydrich (*Ber. deutsch. bot. Gesell.*, **19:** 420 (1901)). A careful examination of the exact dates (as shown above) indicates, however, that the *L. Farlowii* of Heydrich has prior claim, that the *L. Farlowii* Foslie must receive a new name and, further, that the *L. claudescens* Heydrich must be relegated to synonymy.

7. **Lithophyllum elegans** (Foslie) Foslie

Hariot sent certain of the specimens collected by Diguet off La Paz, Mexico, to Foslie, retaining others for his own study. Foslie and Hariot each, independently, gave names to the specimens in their own possession,

Both authors published in 1895, Hariot in the *Journal de Botanique* (vol. 9, pp. 166, 167) and Foslie in the journal of the Norwegian Society ("New or Critical Lithothamnia," *in Det. Kongl. Norske Vidensk. Selsk. Skrifter*, No. 2). The *Lithophyllum elegans* Foslie and the *Lithophyllum margaritae* Hariot undoubtedly are synonymous, but which was first published? Foslie claims (*Det. Kongl. Norske Vidensk. Selsk. Skrifter* 1901, No. 2, p. 20) that *L. elegans* has priority.

8. **Lithophyllum whidbeyense** Foslie

Lithophyllum whidbeyense Foslie ("den. bot. Samling," 5 (1906)) seems to be the same as *L. vancouveriense* Foslie (loc. cit.), judging from our studies of the types and of other collections from the same region. Since the description of *L. whidbeyense* precedes that of *L. vancouveriense* on the same page, that name seems to have a slight precedence.

9. **Heteroderma Nicholsii** nom. nov.

Dermatolithon pustulatum f. *typica* Foslie, "Algol. Notis.," VI, 46 (1909) (p.p.?), *Lithothamnium pustulatum* f. *australis* Foslie, "Remarks on Northern Lithoth.," 117, 128 (1905) (p.p.?), M. B. Nichols, *Univ. Calif. Pub. Bot.*, **3**: 356, pl. 10, figs. 4, 5, pl. 13, figs. 21–24 (1905)!, is to be referred to the genus *Heteroderma* as finally limited by Foslie (Syst. Bemerk., *in* "Algol. Notis.," VI, 56 (1909)). *Heteroderma* seems to be the best solution for referring the very considerable number of non-heterocysted species formerly referred to *Melobesia*. Since *Melobesia* Lamour. (1812) is to be restricted to species with soriform tetrasporangial conceptacles, the majority of the species referred to *Melobesia* seem to fit into *Heteroderma* where Foslie has placed them in his 1909 paper. The type species may be considered to be *Heteroderma subtilissimum* (Foslie) Foslie (loc. cit., 1909, p. 56) from Papua. The genus includes all oligostromatic and non-heterocysted species devoid of a palisade-like hypothallus (*Dermatolithon*), but with the tetrasporangial conceptacles opening by a single pore. The plants which both Nichols and Foslie referred to *Dermatolithon*, from La Jolla, California, are neither of the genus *Dermatolithon* nor of the species *D. pustulatum*. The hypothallus (see Nichols, loc. cit., pl. 13, figs. 21–24) is *not* made up of cells vertically elongated, and the tetrasporangia are regularly 4-parted. A new name is necessary and we dedicate the plant so well described and illustrated by Maurice Barstow Nichols to him, in token of appreciation of his pioneer work among these forms.

10. **Dermatolithon ascripticium** (Foslie) comb. nov.

Dermatolithon pustulatum f. *ascripticia* Foslie, "Algol. Notis.," III, 34 (1906); *Lithophyllum pustulatum* f. *ascripticia* Nichols, *Univ. Calif. Pub. Bot.*, **3**: 354, pl. 10, figs. 2, 3, pl. 11, fig. 10, pl. 12, figs. 18–20 (1909),

This Californian species seems to be independent of both *Dermatolithon macrocarpum* and *D. pustulatum;* from the former it differs in having 4-parted tetrasporangia and from the latter in cell dimensions of the thallus. The type specimens were collected by Mr. Nichols at Santa Catalina Island, California, on *Gelidium pyramidale* N. L. Gardner.

11. **Dermatolithon saxicolum** (Lemoine) comb. nov.

Lithophyllum (*Dermatolithon*) *saxicolum* Lemoine, *Arch. Mus. d'hist. nat., Paris,* **4:** 48, fig. 10 of p. 51 (1929). On stones from 9 meters, Cocos Island, Costa Rica.

As described and figured, this species seems to be related to *Dermatolithon dispar* (Foslie) Foslie, but saxicolous rather than epiphytic. No specimens are available for examination.

12. **Hydrolithon Setchellii** (Foslie) comb. nov.

Goniolithon Setchellii Foslie, "Rev. Syst. Survey Melobesieae," 16 (1900); *Lithothamnium Setchellii* Foslie, "On Some Lithoth.," 18 (1897).

The present species seems to fit better into *Hydrolithon* than into the *Neogoniolithon* (*Goniolithon* of Foslie 1904, non *Goniolithon* subg. *Eugoniolithon* Foslie, 1898). The general habit and structure are in some ways intermediate. The heterocysts are sparse and single, and the hypothallus varies from a single layer (in the main basal portions) to somewhat more complex (in the overlapping lobes). The perithallic cells are somewhat irregularly placed, but do not vary so much in size and arrangement as in *Hydrolithon Reinboldii* (Weber et Foslie) Weber et Foslie.

13. **Litholepis fertilis** (Lemoine) comb. nov.

Melobesia (*Litholepis*) *fertilis* Lemoine, *Arch. Mus. d'hist. nat., Paris,* **4:** 49, fig. 12 on p. 51, pl. 1, fig. 5 (1899); Coiba Island, Panama.

Mme. Lemoine compares the structure to that of *L. mediterranea* Foslie, but considers that it is to be distinguished from all other *Litholepis* species by the size of the (empty) conceptacles (275–500 μ diam.).

Additional new combinations for species of the Pacific coast of North America are to be published elsewhere.

LINEAR PARTIAL DIFFERENTIAL EQUATIONS WITH ANALYTIC COEFFICIENTS

BY FRITZ JOHN

DEPARTMENT OF MATHEMATICS, UNIVERSITY OF KENTUCKY

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This paper contains some general results on linear partial differential equations with analytic coefficients; in particular it is concerned with questions of *uniqueness* of solutions of the Cauchy problem, and with the *functional character* of the solutions.

1. *The Cauchy Problem.*—The general linear mth order equation for a function $u(x_1, \ldots, x_n)$ is given by

$$L[u] = \sum_{i_1 + \ldots + i_n \leq m} A_{i_1 \ldots i_n}(x_1, \ldots, x_n) \frac{\partial^{i_1 + \ldots + i_n}}{\partial x_1^{i_1} \ldots \partial x_n^{i_n}} u = B(x_1, \ldots, x_n) \qquad (1)$$

Only real variables will be admitted. The $A_{i_1 \ldots i_n}$ and B shall be regular analytic functions of those real arguments, wherever considered.[1]

Equation (1) defines at each point $P = (x_1, \ldots, x_n)$ the "characteristic" directions, i.e., those having direction numbers $\alpha_1, \ldots, \alpha_n$ satisfying

$$Q_P(\alpha_1, \ldots, \alpha_n) = \sum_{i_1 + \ldots + i_n = m} A_{i_1 \ldots i_n}(x_1, \ldots, x_n) \alpha_1^{i_1} \ldots \alpha_n^{i_n} = 0 \qquad (2)$$

The *Cauchy problem* consists in determining a solution of (1) for which on a hypersurface S in $x_1 \ldots x_n$-space the "initial values," i.e., the values of $u, \partial u/\partial N, \ldots, \partial^{m-1} u/\partial N^{m-1}$ ($\partial/\partial N$ = normal derivative), are prescribed. The method of power series as applied by Cauchy, Kowalewski and Weierstrass permits to prove the following general theorem:

If S is the image of an open $(n-1)$-dimensional full sphere under a non-singular analytic transformation, and no normal of S has a characteristic direction, and if the initial values are regular analytic on S, then for every closed subset Σ of S there is a neighborhood of Σ in $x_1 \ldots x_n$-space, in which there exists and is uniquely determined a regular analytic solution of (1) taking the prescribed initial values on Σ.[2]

As soon as the restriction to analytic solutions or to analytic initial values is discarded, the behavior of the solutions of the Cauchy problem varies largely with the "type" to which equation (1) belongs; hardly any general results, applying to all types, are known.[3] One of the properties of differential equations, to be examined here, concerns the degree to which solutions behave arbitrarily on any manifold in space. A class F of functions defined in a set R in $x_1 \ldots x_n$-space may be called *arbitrary*, if the following is true: If $\overline{R}$ is any closed subset of R, and P any point of R outside

$\bar{R}$, then there are two functions of F that have the same values in all points of $\bar{R}$, but not in P. In this sense the class of all analytic functions defined in an open set R, or defined on any analytic manifold in $x_1 \ldots x_n$-space, is not arbitrary. On the other hand, the functions of class C^m, where m is any non-negative integer, form an arbitrary class. Similarly arbitrariness can be defined for classes of systems of functions.

It is possible to obtain all solutions of class C^m of (1) by solving certain Cauchy problems with *analytic* initial values for the *adjoint* equation of (1), and by using the *completeness* of the set of analytic functions. This idea was used originally by E. Holmgren[4] for the proof of certain "local" uniqueness theorems. We shall make fuller use of that idea here, chiefly proving uniqueness theorems not restricted to sufficiently small neighborhoods; those only will enable us to make conclusions about the functional behavior of the solutions of (1).

2. *The Fundamental Identity.*—As the main tool we derive an identity of the type of Green's identity for equation (1). Let S_λ denote a family of hypersurfaces given by an equation

$$\lambda = \lambda(x_1, \ldots, x_n) = \text{const.}$$

to be specified later. We define "derived" differential operators $L^{(k)}[u]$ (with respect to λ) to the given operator L by the formulas

$$L^{(0)}[u] = L[u], \; L^{(k+1)}[u] = \lambda L^{(k)}[u] - L^{(k)}[\lambda u]$$

Then

$$L^{(m)}[u] = (-1)^m m! \cdot Q_P\left(\frac{\partial\lambda}{\partial x_1}, \ldots, \frac{\partial\lambda}{\partial x_n}\right) \cdot u, \; L^{(m+1)}[u] \equiv 0 \qquad (3)$$

Let the "adjoint" operator $\bar{L}[u]$ be defined in the usual manner. An invariant element of surface $d\omega$ may be defined by

$$d\omega = \frac{dS_\lambda}{\sqrt{\sum_i \left(\frac{\partial\lambda}{\partial x_i}\right)^2}} = \frac{dx_1 \ldots dx_n}{d\lambda}$$

where dS_λ is the ordinary element of surface of S_λ. The fundamental identity in question then takes the form

$$\int_{S_\lambda} u\bar{L}[w]d\omega = \sum_{k=0}^{m} \frac{1}{k!}\frac{d^k}{d\lambda^k}\int_{S_\lambda} wL^{(k)}[u]d\omega \qquad (4)$$

This identity is invariant under arbitrary coördinate transformations. It can be proved for all "sufficiently regular" families of *closed* surfaces S_λ. It will be used here, however, for cases, where the S_λ are *open* surfaces with a *common boundary*. More exactly (4) is proved for the case that

(*a*) the S_λ are given by the relations

$$\frac{x_1}{1 - \sum_{i=2}^{n} \Sigma x_i^2} = \lambda = \text{const.}, \quad \mu = 1 - \sum_{i=2}^{n} x_i^2 \geqq 0 \tag{5}$$

(*b*) u is of class C^m, and

(*c*) w is of the form $\mu^{m-1}\varphi(\lambda, x_2, \ldots, x_n)$, where λ and μ denote the functions of $x_1, \ldots, x_n$ defined in (5), and φ is of class C^m in $\lambda, x_2, \ldots, x_n$.

3. Uniqueness Theorems.—In applying (4) we do not follow the usual procedure of choosing for w a solution of $\bar{L}[w] = 0$ with a *suitable singularity*, which will yield the value of u at one point. Instead we take for w a solution of the ordinary Cauchy problem

$$\bar{L}[w] = \bar{L}[(1 - \sum_{2}^{n} x_i^2)^{m-1}\varphi] = 0$$

$$\left(\frac{\partial^k \varphi}{\partial \lambda^k}\right)_{\lambda=\epsilon} = \begin{cases} 0 & \text{for } k = 0, \ldots, m-2 \\ v(x_2, \ldots, x_n) & \text{for } k = m-1 \end{cases}$$

According to Cauchy-Kowalewski this Cauchy problem for φ or w will have a solution, if S_ϵ has no characteristic normals, and if v is regular analytic. The solution w can then be shown to be an analytic function of $x_2, \ldots, x_n$, λ, ϵ regular for

$$\sum_{i=2}^{n} x_i^2 \leqq 1, \quad |\lambda - \lambda_0| \leqq \delta, \quad |\epsilon - \lambda_0| \leqq \delta$$

with a certain $\delta > 0$. By integration with respect to λ from λ_0 to ϵ (4) goes over into the following identity, valid for $|\epsilon - \lambda_0| < \delta$:

$$\int_{\lambda_0}^{\epsilon} d\lambda \int_{S_\lambda} w \cdot B(x_1, \ldots, x_n) d\omega + \sum_{k=1}^{m} \frac{1}{k!} \left(\frac{d^{k-1}}{d\lambda^{k-1}} \int_{S_\lambda} w L^{(k)}[u] d\omega \right)_{\lambda=\lambda_0} =$$

$$\frac{1}{m!} \int_{S_\epsilon} \frac{\partial^{m-1}\varphi}{\partial \lambda^{m-1}} \mu^{m-1} L^{(m)}[u] d\omega = (-1)^m \int_{S_\epsilon} \mu^{m-1} Q_P(\alpha_1, \ldots, \alpha_n) \cdot v \cdot u \, d\omega \tag{6}$$

where the $\alpha_i = \dfrac{\partial \lambda}{\partial x_i}$ are direction numbers of the normal of S_ϵ at the point $P = (x_1, \ldots, x_n)$ of S_ϵ. Now the left hand member of (6) depends analytically on ϵ; hence, if u is a solution of (1) of class C^m and $v(x_2, \ldots, x_n)$ is regular, the expression

$$I_v(\epsilon) = \int_{S_\epsilon} \mu^{m-1} Q_P(\alpha_1, \ldots, \alpha_n) \cdot v \cdot u \, d\omega$$

is a regular analytic function of ϵ in a neighborhood of $\epsilon = \lambda_0$, provided S_{λ_0} has no characteristic normals. Furthermore applying (6) to $\lambda_0 = 0$, we

see that $I_v(\epsilon)$ for all sufficiently small ϵ is expressible in terms of u and its derivatives of order $\leqq m - 1$ on S_0, provided S_0 is free of characteristic normals. Moreover, it follows from the Fundamental Lemma of the Calculus of Variations that for a fixed ϵ, u is uniquely determined in all points of S_ϵ, if $I_v(\epsilon)$ is known for all analytic functions v.

Using all these facts one concludes that the initial values of u, $\partial u/\partial N$, $\ldots$, $\partial^{m-1}u/\partial N^{m-1}$ on S_0 uniquely determine u on all S_ϵ, for which none of the surfaces S_λ with $0 \leqq \lambda \leqq \epsilon$ has a characteristic normal. A closer analysis shows that it is sufficient to assume here u to be of class C^{m-1} in the closed set covered by the S_λ with $0 \leqq \lambda \leqq \epsilon$, and to be of class C^m in all interior points of that set. Again, because of the invariance of the characteristic equation (2), the same statement holds, if the hypersurfaces S_λ for $0 \leqq \lambda \leqq \epsilon$, instead of being given by relations (5), can be *transformed into* the hypersurfaces (5) by a non-singular analytic transformation.

The resulting uniqueness theorem for the Cauchy problem for all equations (1) with analytic coefficients is very general, due to the wide choice left for the S_λ. It can roughly be formulated as follows: *The initial values on an analytic hypersurface S_0 uniquely determine u in all points which can be reached by deforming S_0 in such a way that its boundary is kept fixed and all surface elements with characteristic normals are avoided.* This generality is obtained, because the procedure followed here makes it unnecessary to know anything about the characteristic manifolds themselves in advance. In applying this uniqueness theorem to specific cases, it is only necessary to find out how far S_0 can be deformed without violating the restrictions; that will be different for different types of equations.

In this way we find, e.g., for any equation (1) with *constant* coefficients: If C is any *convex* $(n - 1)$-dimensional set in the hyperplane $x_1 = 0$ containing the origin, then the initial values of u on C will uniquely determine u at the point $(1, 0, \ldots, 0)$, if the polar reciprocal set C' of C formed with respect to the unit-sphere about the origin in the $x_2 \ldots x_n$-plane does not contain *in its interior* any point whose coördinates $x_2, \ldots, x_n$ satisfy $Q(1, x_2, \ldots, x_n) = 0$. In the case of *normal-hyperbolic* equations with constant coefficients we may take for C the convex hull of the "wave-surface"; this is in agreement with uniqueness theorems obtained by K. Friedrichs and H. Lewy,[5] and with the explicit solutions constructed by G. Herglotz.[6]

4. Pseudo-Analytic Behavior along an Initial Hypersurface.—From the general uniqueness theorem we can obtain information about the *impossibility* of the Cauchy problem for certain analytic hypersurfaces Σ. That situation will always arise, *if there exists a 2-dimensional plane through the normal of Σ at a point P, which does not contain any direction characteristic at P.* Let A be an n-dimensional neighborhood of P; let s be that part of Σ lying in A, and let A' and A'' be the two *open* sets into which s may divide A. Then in the cases under consideration the *system* of functions

$u, \partial u/\partial N, \ldots, \partial^{m-1}u/\partial N^{m-1}$ is *not arbitrary* on s, if u is assumed to be a solution of class C^m of (1) in A' and to be of class C^{m-1} in $A' + s$; there will indeed exist closed subsets s_0 and s_1 of s without common points, such that the values of the m initial functions in s_0 already uniquely determine the values of u in s_1, as a consequence of the general uniqueness theorem.

Two points are to be observed in this connection: First, that the impossibility of the Cauchy problem is proved *locally*, nothing being assumed about the existence of u outside a neighborhood A of P. Second, that only the *whole system* of initial functions behaves in a non-arbitrary way; u alone might very well be arbitrary on the boundary manifold Σ.

With the help of the geometric test given, it can be seen that the Cauchy data cannot be prescribed arbitrarily on a "surface element" Σ in the following general cases:

(*a*) when (1) is an elliptic equation and Σ any analytic surface element,

(*b*) when (1) is a 2nd order equation, which is neither parabolic nor normal-hyperbolic, and Σ is any analytic surface element,

(*c*) when (1) is a 2nd order normal-hyperbolic equation, and Σ not "space-like," and analytic.[7]

5. Pseudo-Analytic Behavior along Interior Manifolds.—The example of the potential equation suggests that the functional behavior of a solution u of (1) in *interior* points may be much more restricted than in boundary points. Such restricted behavior is indeed made evident by a study of the integrals of u over lower-dimensional manifolds in $x_1 \ldots x_n$-space.

For this purpose we prove the fundamental identity (4) for the more complicated family of hypersurfaces S_λ given by

$$\sum_{\alpha=1}^{s} [x_\alpha - (1 - \sum_{\alpha=s+1}^{n} x_\alpha^2)(c_\alpha - cb_\alpha + \lambda b_\alpha)]^2 = \lambda^2(1 - \sum_{\alpha=s+1}^{n} x_\alpha^2)^2$$

where s is a fixed integer with $0 < s \leqq n$, and the c_α, b_α, c are constants subject to $\sum_{\alpha=1}^{s} b_\alpha^2 < 1$. Then the S_λ for $\lambda > 0$ all have a common $(n - s - 1)$-dimensional boundary given by

$$\sum_{\alpha=s+1}^{n} x_\alpha^2 = 1, \; x_1 = \ldots = x_s = 0$$

and approach for $\lambda, c, c_1, \ldots, c_s$ converging toward 0, the $(n - s)$-dimensional manifold

$$\sum_{\alpha=s+1}^{a} x_\alpha^2 \leqq 1, \; x_1 = \ldots = x_s = 0 \qquad (7)$$

One concludes similarly as before, that for a regular analytic function $v(x_1, \ldots, x_n)$ the expression

$$\int_{S_\lambda} u \cdot v \, d\omega \tag{8}$$

is a regular analytic function of $\lambda, c, b_1, \ldots, b_s$ for sufficiently small positive λ and sufficiently small $c, c_1, \ldots, c_s$, provided no normal of the manifold (7) has a characteristic direction. The following lemma is then applied: If the integrals of a continuous function $F(y_1, \ldots, y_s)$ over spheres in $y_1 \ldots y_s$-space depend analytically on center and radius of those spheres, then F itself is a regular analytic function. This lemma permits to conclude from the analyticity of expressions (8) the following theorem:

If $M_{\lambda_1 \ldots \lambda_s}$ denotes a family of $(n-s)$-dimensional manifolds in $x_1 \ldots x_n$-space, which by a non-singular analytic transformation can be transformed into the manifolds.

$$\begin{cases} x_\alpha = \lambda_\alpha (1 - \sum_{a=s+1}^{n} x_a^2) & \text{for } \alpha = 1, \ldots, s \\ \sum_{a=s+1}^{n} x_a^2 \leqq 1 \end{cases}$$

and if dm denotes any regular analytic element of mass on $M_{\lambda_1 \ldots \lambda_s}$, then

$$\int_{M_{\lambda_1 \ldots \lambda_s}} u \, dm$$

for a solution u of (1) of class C^m in a neighborhood of $M_{\lambda_1 \ldots \lambda_s}$ is a regular analytic function of $\lambda_1, \ldots, \lambda_s$, as long as no normal of the manifold $M_{\lambda_1 \ldots \lambda_s}$ has a characteristic direction.

This theorem may be considered as a generalization to arbitrary equations (1) of the known theorem (which here is included as the special case $s = n$), that if (1) is an elliptic equation, then $u(x_1, \ldots, x_n)$ itself is a regular analytic function.[8]

From the analyticity of expressions (9) we can again conclude that the solution u is not an arbitrary function on certain manifolds. Let P be a point of an r-dimensional analytic manifold M in $x_1 \ldots x_n$-space. *If there is an $(n-r+1)$-dimensional linear space, which contains all normals of M at P, but does not contain any direction characteristic at P, then the solutions of (1), which are of class C^m in an n-dimensional neighborhood of P, do not form an arbitrary class of functions on M itself in a neighborhood of P.* (Here already the function u alone behaves in a non-arbitrary way.[9])

[1] That is, shall be representable by power series locally.

[2] See Courant-Hilbert, *Methoden der mathematischen Physik*, Vol. II, pp. 39, *et seq.*; Hadamard, *Lectures on Cauchy's Problem*, Chap. I.

[3] See the discussion by Hadamard, loc. cit., Chap. II.

[4] Öfversigt af kongl. *Vetenskaps-Akademiens Förhandlinger*, pp. 91–103 (1901); Holmgren considers systems of linear 1st order equations with analytic coefficients for functions of two variables.

[5] *Math. Annalen*, **98**, 192–204 (1928); also Math. Annalen, **104**, 325–339 (1931).

[6] *Abh. Math. Sem. Hamburg. Univ.*, **6** (1928); *Ber. d. sächs. Akad.*, **78** (1926) and **80** (1928). See also Courant-Hilbert, loc. cit., pp. 455, *et seq.*

[7] See on necessary or sufficient conditions for the Cauchy problem:

For the potential equation: Hadamard, loc. cit., p. 31, sec. 15 bis.

For the wave equation on time-like manifolds: Hadamard, loc. cit., pp. 349–357.

For hyperbolic equations with 3 independent variables: E. W. Titt, *Ann. Math.*, **40**, 862–891 (1939).

For a certain ultra-hyperbolic equation: G. Owens, *Duke Math. Jour.*, **9**, 271–282 (1942).

[8] See Holmgren, loc. cit., 1901, pp. 437–456. S. Bernstein, *Math. Annalen*, **59**, 20–76 (1904). T. Rado, *Math. Zeit.*, **25**, 514–589 (1926). H. Lewy, *Math. Annalen*, **101**, 609–619 (1929); *Trans. Am. Math. Soc.*, **37**, 417, *et seq.* (1935). E. Hopf, *Math. Zeit.*, **34**, 194–233 (1931).

[9] Special known instances of non-arbitrary behavior in interior points are: In the case of ultra-hyperbolic equations with constant coefficients: Courant-Hilbert, loc. cit., pp. 427–430; in the case of time-like manifolds for the "equation of Darboux": F. John, *Math. Annalen*, **113**, 541–559 (1935).

GROUPS CONTAINING A PRIME NUMBER OF CONJUGATE SUBGROUPS

By G. A. Miller

Department of Mathematics, University of Illinois

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While there are many groups which have the property that each of them contains one and only one invariant proper subgroup there is no group which contains one and only one non-variant subgroup since a non-invariant subgroup is transformed under the group into another such subgroup of this group. The smallest number of non-invariant subgroups of a group is therefore two and when a group contains exactly two non-invariant subgroups they are necessarily conjugate under the group. Similarly when a group contains exactly three non-invariant subgroups they must all be conjugate under the group but when a group contains more than three non-invariant subgroups they may appear in more than one set of conjugates under the group. For instance, the group of the square contains four non-invariant subgroups which appear in two sets of conjugates under the group. It should be noted that a non-invariant subgroup of a group is necessarily a proper subgroup of it.

It is not difficult to construct an infinite system of groups of order p^m, p being any prime number, which has the property that every group contained therein involves exactly p non-invariant subgroups and that these subgroups constitute a single set of conjugates under the group. To construct such a system we may start with the cyclic group of order

p^{m-1}, $m > 3$, and extend this group by an operator of order p which transforms this cyclic group into itself and gives rise to a commutator of order, p. This extended group of order p^m contains $p + 1$ subgroups of order p, including the commutator subgroups of this order, which constitutes the central of the group. The remaining subgroups of order p are the p conjugate subgroups under the group of order p^m, which is conformal with the abelian group of order p^m and of type 1, $m - 1$. Every operator of this group whose order exceeds p generates the commutator subgroup of the group and every subgroup which contains such an operator is invariant.

When p is odd it is only necessary to assume that $m > 2$ in the preceding paragraph since the group of order p^3 will then also satisfy the condition that it contains exactly p non-invariant subgroups which constitute a single set of conjugate subgroups under the group, but when $p = 2$ there result two corresponding groups of order 8. One of these is the octic group and contains four non-invariant subgroups of order 2 which are conjugate in pairs, as was noted above. The other is the quaternion group, which involves no non-invariant subgroup but is also non-abelian. We shall prove in what follows that when $p = 2$ the given infinite system of groups includes all the groups which separately contain two and only two non-invariant subgroups but when p is odd there are other infinite systems composed of groups which separately involve exactly p conjugate subgroups.

Suppose now that the group G contains exactly two non-invariant subgroups. As each of these two subgroups is invariant under half the operators of G there must be a subgroup H of index 2 under G which involves this subgroup. The subgroup H must also contain the other non-invariant subgroup of G since this subgroup is also transformed into itself by exactly half of the operators of G and the operators of G which do not transform into itself the first of the two given subgroups must transform this subgroup into the second of these two subgroups and hence they do not transform this second subgroup into itself. That is, *every group which contains two and only two non-invariant subgroups contains a subgroup of index 2 which involves these two subgroups invariantly while each of the remaining operators of the group transforms these two subgroups into each other.*

Since all the subgroups of H are invariant under H it results that H is either abelian or Hamiltonian. It cannot contain more than two subgroups which are invariant under G because G is supposed to contain two and only two non-invariant subgroups. Hence it results that when H is Hamiltonian its order is a power of 2 and the order of G is twice the order of H. It is known that a Hamiltonian group whose order is a power of 2 is the direct product of the quaternion group and the abelian group of order 2^m and of type 1^m and that it contains a characteristic subgroup of order 2^{m+1} which is abelian and of type 1^{m+1} and involves all the operators of order 2 contained in this Hamiltonian group. Hence m could not exceed

zero. As it is known that a group of order 16 does not contain two and only two non-invariant subgroups it results that H is abelian whenever G contains two and only two non-invariant subgroups.

The operators of G which are not in H must include at least one whose order is a power of 2 since H is a subgroup of index 2 under G. Hence H cannot involve a Sylow subgroup of odd order since all the subgroups of G which are not contained in H are invariant under G. It therefore results that the order of G is a power of 2. As H involves at least two subgroups of the same order it cannot be cyclic. It cannot have more than two invariants since not more than two of its subgroups are invariant under G and G contains only two non-invariant subgroups. For the same reason one of the independent generators of H must be of order 2 and each of the operators of G which are not H generates the same subgroup of order 2. The two non-invariant subgroups found in G are therefore of order 2 and all the operators of G which are not in H are of order 2^{m-1}, if the order of H is 2^{m-1}. It therefore follows that G belongs to the infinite system of groups noted above and there results the following theorem: *If a group contains two and only two non-invariant subgroups it is of order 2^m and it is conformal with the abelian group of type 1, $m-1$. There is one and only one such group for every value of $m > 3$ and its commutator subgroup is of order 2.*

Suppose that a group G contains p conjugate subgroups, p being a prime number, and that all of its other subgroups are invariant. These conjugate subgroups are transformed under G according to a permutation group of degree p which has no more than p subgroups. Such a group involves only one subgroup of order p, since the subgroups of order p in this permutation group are Sylow subgroups, and if there were more than one such Sylow subgroup in it there would be at least $p + 1$. It therefore results that if a group contains a set of p conjugate subgroups while all of its other subgroups are invariant it must be either isomorphic with a permutation of degree p which contains an invariant subgroup of order p or it contains an invariant subgroup of index p which includes all of its non-invariant subgroups as invariant subgroups. In particular, *if a group contains a prime number of conjugate subgroups while all of its other subgroups are invariant then either no two of these subgroups transform each other into themselves or every two of these subgroups transform each other into themselves.*

When every two of the p conjugate subgroups of G transform each other into themselves, then G contains an invariant subgroup H of index p which involves these p subgroups invariantly and contains no non-invariant subgroup. Hence this invariant subgroup is either abelian or Hamiltonian. It is easy to prove that it could not be Hamiltonian since every Hamiltonian group contains a characteristic subgroup of order 2 and hence could not involve exactly an odd prime number of non-invariant subgroups. It therefore results that H is abelian and that the order of H is a power of p since

the operators of G which are not in H include at least one whose order is a power of p. The facts that H cannot have more than two invariants, cannot be cyclic and when it has two invariants, one of them is p, follow exactly in the same way when p is an odd prime number as when $p = 2$. It therefore results that whenever every two of the p non-invariant conjugate subgroups transform each other into themselves then G belongs to the infinite system of groups considered in the second paragraph of this article.

It remains to consider the case when no two of the conjugate subgroups of G transform each other into themselves and hence G involves an invariant subgroup which gives rise to a quotient group which is simply isomorphic with a non-cyclic transitive group of degree p involving an invariant subgroup of order p. In the simplest case this transitive group is the symmetric group of degree 3 and all the possible groups can be obtained by establishing a dimidiation between this group and the cyclic group of order 2^m. Moreoever, each of the groups thus obtained satisfies the condition that it contains three and only three conjugate subgroups such that no two of these subgroups transform each other into themselves. This completes the determination of all the group which involve three and only three non-invariant subgroups.

Every transitive group of degree p which involves an invariant subgroup of order p is known to contain p and only p non-invariant subgroups whenever its order is pq, q being a prime divisor of $p - 1$, and only then. By establishing a p, $q^{\alpha-1}$ isomorphism between this transitive group and the cyclic group of order q^α, $\alpha > 1$, there results a group of order pq^α which satisfies the condition that it contains p conjugate subgroups and that each of its other subgroups is invariant. This completes the determination of all the groups which separately contain a prime number of conjugate subgroups while all of their other subgroups are invariant.

NEW CHARACTERIZATIONS OF SEGMENTS AND ARCS

BY LEONARD M. BLUMENTHAL

DEPARTMENT OF MATHEMATICS, UNIVERSITY OF MISSOURI

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I. The writer has for some time been interested in studying the metric and topological properties of various classes of metric spaces when these spaces are assumed to be *free from equilateral k-tuples*. It has been shown, for example, that a complete, convex, externally convex metric space M (containing at least two points) is metrically a straight line if and only if M

does not possess an equilateral triple.[1] Indeed, any metric space containing a line L and a point not belonging to L has an equilateral triple.

On the topological side, one inquires what topological properties a space must possess in order that it may be homeomorphic to a space with prescribed metric properties. The metrization problem is subsumed under this general class of problems as a "first case."

In this note two new theorems belonging to such a *Programme* are announced and their proofs briefly sketched. One of the theorems was conjectured by the writer in a paper now in press, and the other is closely related to the metric characterization of the line cited above.[2]

II. *Characterization Theorems.*

THEOREM 1. *A compact convex metric space M of at least two points is congruent with a line segment if and only if M is free from equilateral triples.*

Proof. If M is congruent with a line segment, then obviously M is free from equilateral triples. Assuming M free from such triples, we note that M contains two points p, q at maximum distance and (since M is convex) a segment (p, q) (i.e., a set of points congruent with a line segment) with end-points p and q. We suppose M has a point r not belonging to (p, q) and show this implies the existence of an equilateral triple.

Case 1. There exists an interior point s of (p, q) such that a segment with end-points r and s contains neither of the subsegments (p, s), (s, q) of (p, q).

Then (r, s) has a point r^*, with arbitrarily small positive distance from (p, q), such that a point r_0^* of (p, q) nearest r^* is an interior point of (p, q). The method of a previous paper may now be applied to prove the existence of two points on (p, q) which, together with r^*, form an equilateral triple.[3]

Case 2. The situation described in Case 1 does not hold.

It follows that a point s of (p, q) with maximum distance d from r is interior to (p, q) and hence each segment (r, s) contains either (p, s) or (q, s). Selecting the labeling so that $(p, s) \subset (r, s)$, we have $rp + ps = rs = d$. It is easy to show that for each interior point t of the subsegment (q, s), any segment (r, t) contains the subsegment (q, t) and hence, letting t approach s, it follows that q is interior to a segment (r, q, s) of length d.

Clearly $pq = ps + sq = d - pr + d - rq = 2d - (pr + rq)$. Since pq is a maximum distance in M, we have $pq \geq d$ and hence $d \geq pr + rq$. On the other hand, $pq \leq pr + rq \leq d$, and so $pq = d$ and r is between p and q. It is easily shown that the segments (r, p, s) and (r, q, s) have no points other than r and s in common.

Let, now, t and v be points of (r, p, s) and (r, q, s), respectively, such that $rt = rv = 2d/3$. We observe that $v \in (r, q)$ readily implies $t \in (p, s)$.[4] If v and t are end-points of a segment containing neither (p, t) nor (t, q) the presence of an equilateral triple with v as one vertex follows as in Case 1.[5] Suppose, then, that any segment joining v to t contains either (t, q) or (p, t). If such a segment contains (t, q), then $vt = ts + sv = 2d/3$. The other

possibility is easily seen to lead to a contradiction, and the theorem is proved.

THEOREM 2. *A metric Peano continuum without an equilateral triple is an arc.*

Proof. It suffices to show that the continuum contains neither a simple closed curve nor a tripod (i.e., three arcs which have only a single point—an end-point of each—in common). Since such figures are one-dimensional continua, they may, according to a theorem of Beer,[6] be *convexified* (i.e., a topologically equivalent metric may be introduced in terms of which the figures are metrically convex). Applying Theorem 1 to the convexified figures it is seen that they surely contain equilateral triples (else they would be segments and the original figures arcs). A close examination of Beer's procedure leads one to conclude that if equilateral triples are present in the convexified simple closed curve or tripod, then such triples occur in the original metric, and the theorem is established.

[1] Blumenthal, L. M., and Robinson, C. V., "A New Characterization of the Straight Line," *Reports of a Mathematical Colloquium*, 2nd Ser., Issue 2, 25–28 (1940).

[2] Blumenthal, L. M., "Some Imbedding Theorems and Characterization Problems of Distance Geometry," *Bull. Amer. Math. Soc.* (in press).

[3] See reference 1.

[4] If $v \in (q, s)$ then $t \in (r, p)$ or $t \in (p, s)$. The first case differs only in labeling from the one discussed, while in the second case we have immediately $vt = 2d/3$.

[5] The cases (*a*) $p = t$ and (*b*) $v = q$ offer no difficulties.

[6] Beer, G., "Beweis des Satzes, dass jede im kleinen zusammenhängende Kurve konvex metrisiert werden kann," *Fundamenta Mathematicae*, **31**, 281–320 (1938).

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*SOME PRELIMINARY STUDIES ON THE MECHANISM OF VIRUS MULTIPLICATION**

BY JOHN SPIZIZEN

WM. G. KERCHOFF LABORATORIES IN THE BIOLOGICAL SCIENCES
CALIFORNIA INSTITUTE OF TECHNOLOGY AND VANDERBILT UNIVERSITY

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The most distinctive characteristic of the process of virus multiplication is its dependence on the integrity and active growth of the infected host cells (e.g., Findlay and MacCallum[1]). Except for some studies on the enzymic complement of vaccinia virus,[2, 3] nothing is known concerning the mechanism of this dependence. The following is a preliminary account of some studies designed to investigate this problem.

In order to approach this problem, it was necessary first of all to establish criteria which would distinguish the general metabolic reactions of the

cell associated with normal cellular activity from those reactions specifically involved in virus multiplication. This is extremely difficult to do in the cells of higher animals and plants. Bacteriophage, the virus of bacteria, was found to be suitable material for such an approach, for the end result of the overall, normal metabolic activity of the host cells is multiplication, which can be measured very simply in culture. Hence, it is possible, by interfering with or enhancing the level of metabolism of the cell infected with virus, to determine concomitantly the extent of the effect, if any, on the multiplication of the virus.

Relation between Cell Growth and Virus Multiplication.—The viruses studied were two strains of anti-*Escherichia coli* bacteriophage, P_1[4] and γ.[5]

An extensive study was made of virus P_1 in regard to the influence of various substrates on virus and cell growth.[6, 7, 8] A number of amino-acids and closely related compounds were found capable of supporting both cell and virus growth. In general, whenever cell growth occurred concomitant virus multiplication took place. Two exceptions to this were found, namely, in the case of glycine and glycine anhydride (2,4-diketopiperazine). These substances, in low concentrations, were insufficient by themselves for cell multiplication, but supported quite considerable virus multiplication (table 1).

TABLE 1

CONCENTRATION RANGE OF GLYCINE AND GLYCINE ANHYDRIDE IN WHICH P_1 MULTIPLICATION OCCURRED, BUT NO B_1 GROWTH (FOR 135 MINUTES)

GLYCINE	GLYCINE ANHYDRIDE
5×10^{-4} *M* to 5×10^{-3} *M*	2×10^{-4} *M* to 3×10^{-3} *M*

NOTE: At 5×10^{-3} *M* glycine and 3×10^{-3} *M* glycine anhydride, the virus multiplication (step-size in 60 minutes) was practically optimum.

In another series of studies designed to investigate the influence of metabolic inhibitors on virus multiplication, it was found that in a certain range of concentrations of sodium arsenite, the growth of virus γ on its host in a

TABLE 2

MULTIPLICATION OF VIRUS γ AND HOST CELLS (60 MINUTES) IN AN ASPARAGINE-GLUCOSE-PHOSPHATE MEDIUM WITH VARIOUS CONCENTRATIONS OF SODIUM ARSENITE ADDED 8 MINUTES AFTER INFECTION (HOST CELLS PREVIOUSLY GROWN IN THE SYNTHETIC MEDIUM)

	CONCENTRATION OF SODIUM ARSENITE (*M*)									
	0	5×10^{-7}	2.5×10^{-6}	5×10^{-6}	7.5×10^{-6}	1×10^{-5}	1.5×10^{-5}	2×10^{-5}	2.5×10^{-5}	5×10^{-5}
γ Multiplication	80	80	80	80	60	25	1	1	1	.1
B Growth	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	1.5

highly purified asparagine-glucose-phosphate medium[9] was completely inhibited, while the host cells multiplied at their normal rate (the host cells being in the logarithmic phase) (table 2).

To sum up, then, it is possible to separate the process of virus multiplication from the growth of the host cells. Under certain conditions, cell growth may proceed unhindered while virus multiplication is inhibited completely. Under other conditions virus multiplication may proceed at a normal rate while cell divisions are inhibited.

Effect of Metabolic Inhibitors and Some Substrates on Virus Multiplication.—In order to understand the kind of metabolic reactions which are associated with virus multiplication in the cell, a survey was made of the effect of various metabolic poisons on virus growth when no cell multiplication occurred, as in certain concentrations of glycine and glycine anhydride (table 3).

TABLE 3

INFLUENCE OF METABOLIC POISONS ON VIRUS P_1 MULTIPLICATION IN 8.7×10^{-4} *M* GLYCINE ANHYDRIDE

INHIBITOR	CONC. (*M*)	% INHIBITION OF VIRUS MULTIPLICATION (100 MIN.)
Sodium cyanide	2×10^{-3}	100
Iodoacetic acid	5×10^{-4}	100
Sodium arsenite	6×10^{-4}	100
Phlorizin	2×10^{-3}	0
2,4-Dinitrophenol	5×10^{-4}	100
p-Aminophenol	1×10^{-3}	100
Arsenic pentaoxide	5×10^{-4}	40
Urethane	1×10^{-3}	0
Sodium fluoride	2.4×10^{-3}	0
Sodium sulfite	4×10^{-4}	0
Malonic acid	1×10^{-2}	0
Sodium pyrophosphate	2.5×10^{-4}	0

Hence, cyanide, iodoacetate, arsenite, dinitrophenol, and *p*-aminophenol appear to inhibit reactions associated rather closely with virus P_1 multiplication.

The influence of a large number of substrates on virus P_1 propagation in 8.7×10^{-4} *M* glycine anhydride was also studied, under conditions where there was no considerable effect on the cell multiplication. The effect of some of the more effective substrates is summarized in table 4.

These results suggest that the multiplication of virus P_1 is associated with certain specific cellular reactions known to be involved in the respiratory nexus of the cell. More detailed studies with these and other metabolic poisons and substrates may yield more precise data as to the kind of reactions involved in this and other viruses. Such studies are of prime importance for the investigation of possible therapeutic measures for virus diseases.

TABLE 4

INFLUENCE OF SOME SUBSTRATES ON VIRUS P_1 MULTIPLICATION IN 8.7×10^{-4} *M* GLYCINE ANHYDRIDE

(Bacterial multiplication not appreciably influenced in all cases except yeast nucleic acid)

SUBSTRATE	CONC. (*M*)	% INCREASE IN P_1 (100 MIN.)
α-Glycerophosphoric acid	6×10^{-4}	150
Glucose-6-phosphate	4×10^{-4}	50
Adenosine triphosphate	2×10^{-4}	85
Coenzyme I	1×10^{-4}	80
Adenylic acid	3×10^{-4}	26
(Guanylic acid	3×10^{-4}	0)
Yeast nucleic acid	Less than 1×10^{-5}	350
Oxaloacetic acid	7.5×10^{-4}	200
α-Ketoglutaric acid	7×10^{-4}	260
Succinic acid	8.5×10^{-4}	95
Fumaric acid	8.5×10^{-4}	56
Calcium hydrogen malate	5.5×10^{-4}	145
Uric acid	5×10^{-4}	100
Xanthine	6.5×10^{-4}	15

The Arsenite Effect.—It is evident from table 2 that concentrations of 7.5×10^{-5} *M* and over of sodium arsenite are sufficient to inhibit the multiplication of virus γ in an asparagine medium (100% inhibition at 1.5×10^{-6} *M*), but bacterial growth cannot be inhibited with less than about 5×10^{-5} *M*. This is true when arsenite is added to virus-infected cells 8 minutes after infection, but not when the arsenite is added sooner (table 5).

TABLE 5

INFLUENCE OF PREVIOUS CONTACT OF HOST CELLS WITH ARSENITE ON γ MULTIPLICATION IN AN ASPARAGINE-GLUCOSE MEDIUM

HISTORY OF HOST CELLS	γ MULTIPLICATION IN ARSENITE CONCS. OF (*M*)						
		2.5×10^{-6}	5×10^{-6}	1×10^{-5}	1.5×10^{-5}	2.5×10^{-5}	5×10^{-5}
24 Hours in 2.5×10^{-5} *M* sodium arsenite before infection	94	98	..	92	96	92	..
In 1.5×10^{-5} *M* arsenite 2 minutes before infection with γ and for 8 minutes thereafter	59	..	59	59	45	17	1

NOTE: Differences in virus multiplication figures for 0 arsenite in the two series are due to the difference in the number of infected cells in the two experiments, and not to the effect of the previous history.

From table 5 (cf. also table 2) it is evident that the longer the cells are exposed to arsenite previous to infection with virus the less effect the same

concentration of arsenite will have on virus γ multiplication. However, previous exposure of the cells to arsenite does not appear to influence the ability of the cells to support γ multiplication in the absence of arsenite. (In all cases cited there appeared to be no influence on the bacterial growth.)

Additional experiments designed to investigate the nature of the arsenite effect indicated that the arsenite effect is *instantaneous*, as was suggested by the fact that previous exposure of the cells to arsenite for 2 to 10 minutes altered the influence of various low concentrations on γ multiplication. Thus, when arsenite was added to a mixture of growing cells and virus at different times during the latent period of virus growth, there was a definite inhibition of virus multiplication. Even when arsenite (1.5×10^{-5} M and 2.5×10^{-5} M) was added 20 minutes after infection (one minute before the end of the latent period of γ multiplication under these conditions, after which there is a rapid release of virus) there is about 60% inhibition of virus growth.

On the other hand, the arsenite inhibition of virus growth can be relieved almost instantly on its removal. When arsenite (2.5×10^{-5} M) was added to cells 2 minutes prior to infection with virus γ, and replaced with fresh asparagine-glucose medium containing no arsenite at 25 minutes after infection, the step-size value[4] for virus growth was almost the same as if no arsenite had been present to begin with.

These experiments need extension, but certain conclusions are already evident. Arsenite appears to have a somewhat more specific effect on the virus than on the cell growth. The inhibiting action of arsenite on virus growth is readily relieved by replacing the arsenite with fresh medium lacking arsenite. The arsenite effect is extremely rapid, for it is capable of stopping the release of most of the virus by the cells at the end of the latent period of virus multiplication. Finally, the cell appears to be capable of "adapting" itself to the presence of arsenite, at least as far as the processes which lead to virus propagation are concerned.

The importance of understanding the mechanism of the arsenite effect cannot be underestimated. It is intimately concerned with the problem of the identity of the metabolic reactions involved in virus multiplication, some of which at least may not be involved in cell growth. The identification of the reactions influenced by arsenite may be studied by classical biochemical methods. As far as is known, no such studies have been made with bacteria. Krebs[10] and Borsook and Dubnoff[11] studied the effect of arsenite on metabolic systems in sliced mammalian kidney tissue, and concluded that arsenite is an inhibitor of the reactions involved in the oxidation of α-keto acids. Whether this is true for bacteria remains to be seen.

Summary.—The processes of virus multiplication and cell growth can be separated experimentally in the two bacterial viruses and their corre-

sponding hosts studied. Under conditions in which virus multiplication proceeds in the absence of cell growth, it was found that certain specific metabolic poisons (cyanide, iodoacetate, arsenite, dinitrophenol, *p*-aminophenol) would inhibit virus growth, while others did not. Certain substances known to be involved either as intermediates or as coenzymes in intermediary carbohydrate metabolism in the cell were shown to enhance virus multiplication in the absence of bacterial growth.

Finally, arsenite was found to be a specific inhibitor of the multiplication of virus γ. The study of this inhibition may give valuable results concerning the nature of the reactions involved in virus multiplication.

* Part of this work was performed during the tenure of a National Research Council Fellowship in the Medical Sciences. Present address: Department of Bacteriology, Loyola University, School of Medicine, Chicago, Ill.

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[2] Parker, R. F., and Smythe, C. V., *Jour. Exp. Med.*, **65,** 109 (1937).

[3] Hoagland, C. L., *et al.*, *Ibid.*, **72,** 139 (1940); **71,** 737 (1940); **74,** 769 (1941); **74,** 133 (1941).

[4] Active on a strain of *Escherichia coli* (B_1) originally studied by Ellis, E. L., and Delbruck, M., *Jour. Gen. Physiol.*, **22,** 365 (1939).

[5] From the original *PC* of Kalmanson, G. M., and Bronfenbrenner, J., *Ibid.*, **23,** 203 (1939), active on another strain of *Es. coli.*

[6] Ellis, E. L., and Spizizen, J., *Science*, **92,** 91 (1940).

[7] Spizizen, J., *Jour. Biol. Chem.*, **140,** cxxiv (1941).

[8] Spizizen, J., Thesis, California Institute of Technology, 1942.

[9] So-called "chemically pure" asparagine may often contain significant amounts of thiamin and biotin, as well as traces of other biologically active substances. Hence in this work asparagine was repeatedly crystallized before use. An ammonia-glucose-phosphate medium was also found to be sufficient for host and virus growth when a magnesium or calcium salt was present.

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THE DETERMINATION OF L.D.50 AND ITS SAMPLING ERROR IN BIO-ASSAY, II

BY EDWIN B. WILSON AND JANE WORCESTER

DEPARTMENT OF VITAL STATISTICS, HARVARD SCHOOL OF PUBLIC HEALTH

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If a bio-assay[1] were made at three dilutions D_1, $D_2 = aD_1$, $D_3 = a^2D_1$ and if the probabilities P_1, P_2, P_3, assumed to be in increasing sequence in the universe but with fluctuations due to sampling, were observed, the growth curve

$$P = {}^1/_2 + {}^1/_2 \tanh \alpha(x - \gamma) \qquad (1)$$

containing the two parameters α, γ could be fitted to the three observed proportions P_1, P_2, P_3, corresponding to the three values of the logarithmic dose x_1, x_2, x_3, which are in arithmetical progression with the difference $c = \log a$. The natural method to use would be R. A. Fisher's method of maximum likelihood.[2] We shall use the middle dilution as a point of reference $x_2 = x$ with the other two at $x - c$, $x + c$; then the probability of the observations s_1, s_2, s_3 in the three series is

$$\frac{(n!)^3 P_1^{s_1} P_2^{s_2} P_3^{s_3} Q_1^{n-s_1} Q_2^{n-s_2} Q_3^{n-s_3}}{s_1!\ s_2!\ s_3!\ (n-s_1)!\ (n-s_2)!\ (n-s_3)!},$$

where $Q_i = 1 - P_i$ and P_i is taken from (1); and its natural logarithm, the likelihood, is (except for a constant which does not depend on α or γ)

$$L = \Sigma s_i \log [1 + \tanh \alpha(x_i - \gamma)] + \Sigma(n - s_i) \log [1 - \tanh \alpha(x_i - \gamma)]. \qquad (2)$$

The derivatives with respect to α and γ are

$$\frac{\partial L}{\partial \gamma} = -n\alpha\Sigma(2P_i - 1) + n\alpha\Sigma \tanh \alpha(x_i - \gamma), \qquad (3)$$

$$\frac{\partial L}{\partial \alpha} = n\Sigma(2P_i - 1)(x_i - \gamma) - n\Sigma(x_i - \gamma) \tanh \alpha(x_i - \gamma). \qquad (4)$$

Placing x_1, x_2, x_3 equal to $x - c$, x, $x + c$ and setting the derivatives equal to zero we have

$$\Sigma(2P_i - 1) = \tanh \alpha(x - c - \gamma) + \tanh \alpha(x - \gamma) + \tanh \alpha(x + c - \gamma), \qquad (5)$$

$$(2P_1 - 1)(x - c - \gamma) + (2P_2 - 1)(x - \gamma) + (2P_3 - 1)(x + c - \gamma) = (x - c - \gamma) \tanh \alpha(x - c - \gamma) + (x - \gamma) \tanh \alpha(x - \gamma) + (x + c - \gamma) \tanh \alpha(x + c - \gamma).$$

The first equation may be multiplied by $x - \gamma$ and subtracted from the second; then

$$2(P_3 - P_1) = -\tanh \alpha(x - c - \gamma) + \tanh \alpha(x + c - \gamma). \qquad (6)$$

We have to solve (5) and (6) for α and γ.

Let $A = \Sigma(2P_i - 1)$, $B = P_3 - P_1$, and expand the tanh functions setting $X = \tanh \alpha(x - \gamma)$, $C = \tanh \alpha c$. Then

$$A = \frac{X - C}{1 - XC} + X + \frac{X + C}{1 + XC} = \frac{3X - 2XC^2 - X^3C^2}{1 - X^2C^2}, \qquad (7)$$

$$2B = -\frac{X - C}{1 - XC} + \frac{X + C}{1 + XC} = \frac{2C(1 - X^2)}{1 - X^2C^2}. \quad (8)$$

Or

$$C^2[X^3 - AX^2 + 2X] = 3X - A,\ C^2BX^2 + C(1 - X^2) = B. \quad (9)$$

Eliminating C, the quantity X is determined from the cubic

$$3X^3 - 4AX^2 + (6 + A^2 - 4B^2)X - 2A = 0. \quad (10)$$

Given the numerical values of A and B from the observations, the cubic may be solved numerically by any method of approximation, but for most cases the result

$$X = \frac{4A}{9} - \frac{b}{a} + \frac{729}{a}\left(\frac{b}{a}\right)^3, \begin{cases} a = 1458 - 189A^2 - 972B^2 \\ b = 162A - 20A^3 - 432AB^2 \end{cases} \quad (11)$$

is sufficient, and often the third term may be omitted. Then[3]

$$\alpha = \frac{1}{c}\tanh^{-1}\frac{2B}{X^2 - AX + 2},\ \gamma = x - \frac{c\tanh^{-1}X}{\tanh^{-1}\dfrac{2B}{X^2 - AX + 2}}. \quad (12)$$

For example, if $n = 20$ and $s_1 = 8$, $s_2 = 15$, $s_3 = 20$ in $^1/_2$ dilutions so that $c = 0.6931$ (using natural logarithms), $P_1 = 0.40$, $P_2 = 0.75$, $P_3 = 1.00$, $A = 1.30$, $B = 0.60$,

$$X = 4\frac{1.30}{9} - \frac{-35.516}{788.67} + \frac{729}{788.67}\left(\frac{-35.516}{788.67}\right)^3 =$$

$$0.57778 + 0.04503 - 0.00008 = 0.62273,$$

$$\alpha = \frac{1}{c}\tanh^{-1}(0.7603),\ \gamma = x - c\frac{\tanh^{-1}0.6227}{\tanh^{-1}0.7603}.$$

As good tables of the $\tanh^{-1}$ function may not be at hand one may use the logarithmic equivalent

$$\tanh^{-1} = {}^1/_2\log_e\frac{1 + x}{1 - x},\ \alpha = \frac{1}{2c}\log_e\frac{1.7603}{0.2397},\ \gamma = x - c\frac{\log_e\dfrac{1.6227}{0.3773}}{\log_e\dfrac{1.7603}{0.2397}}$$

With $c = 0.6931$ we have $\gamma = x - 0.5071$, $\alpha = 1.438$. For many purposes the table of hyperbolic functions in B. O. Peirce's *Short Table of Integrals*, page 126 (1929) may be adequate; natural logarithms may be replaced by logarithms to the base 10 if x, c, α, γ are all expressed logarithmically to that base.

R. A. Fisher's formula for the standard errors of the parameters calls for the mean values of the second derivatives of L. There are

$$\frac{\partial^2 L}{\partial \gamma^2} = -n\alpha^2 \Sigma \operatorname{sech}^2 \alpha(x_i - \gamma) = -4n\alpha^2 \Sigma P_i Q_i,$$

$$\frac{\partial^2 L}{\partial \alpha^2} = -n\Sigma(x_i - \gamma)^2 \operatorname{sech}^2 \alpha(x_i - \gamma) = -4n\Sigma P_i Q_i (x_i - \gamma)^2,$$

$$\frac{\partial^2 L}{\partial \alpha \partial \gamma} = n\alpha\Sigma(x_i - \gamma) \operatorname{sech}^2 \alpha(x_i - \gamma) = 4n\alpha\Sigma P_i Q_i (x_i - \gamma)$$

where the values of P_i are taken from the fitted curve rather than from the sample. The Hessian

$$H = \begin{vmatrix} \frac{\partial^2 L}{\partial \gamma^2} & \frac{\partial^2 L}{\partial \alpha \partial \gamma} \\ \frac{\partial^2 L}{\partial \alpha \partial \gamma} & \frac{\partial^2 L}{\partial \alpha^2} \end{vmatrix} = \frac{\partial^2 L}{\partial \gamma^2} \frac{\partial^2 L}{\partial \alpha^2} - \left(\frac{\partial^2 L}{\partial \alpha \partial \gamma} \right)^2$$

is then formed and the standard errors are[4]

$$\sigma_\alpha^2 = -\frac{1}{H} \frac{\partial^2 L}{\partial \gamma^2}, \quad \sigma_\gamma^2 = -\frac{1}{H} \frac{\partial^2 L}{\partial \alpha^2}.$$

The correlation between sampling variations in γ and α is by Fisher's formula

$$r_{\alpha\gamma} = \frac{\partial^2 L}{\partial \alpha \partial \gamma} \div \sqrt{\frac{\partial^2 L}{\partial \alpha^2} \frac{\partial^2 L}{\partial \gamma^2}}.$$

It is not often that one wishes this value, but there is an interesting connection between the standard error that would be found for γ if α were considered as known and the standard error found on the basis of no such assumption which may be exhibited in terms of r. For if α were taken as known

$$\sigma_\gamma^2 = (-\partial^2 L / \partial \gamma^2)^{-1}$$

and

$$\frac{\sigma_\gamma^2, \ \alpha \text{ known}}{\sigma_\gamma^2, \ \alpha \text{ unknown}} = \frac{H}{\frac{\partial^2 L}{\partial \gamma^2} \frac{\partial^2 L}{\partial \alpha^2}} = 1 - r^2.$$

The value of r is zero when $\Sigma P_i Q_i (x_i - \gamma) = 0$, and this will nearly vanish whenever the probabilities on the fitted line are nearly symmetric with

respect to the middle dilution[5] (the middle dilution being near the 50% point).

According to the conventions of Least Squares, the weight of an observation is proportional to the reciprocal of the square of its standard error. If we could consider the determination of γ on the assumption that α is known (or that there happens to be no correlation between α and γ), we should have

$$\frac{1}{\sigma_\gamma^2} = -\frac{\partial^2 L}{\partial \gamma^2} = 4n\alpha^2 \Sigma P_i Q_i.$$

Hence the weight contributed to the determinaton of γ by each point on the curve is proportional to $4P_iQ_i$ and will be relatively small for those values of P which are near 0 or 1. Thus the addition of dilutions of very high or of very low strengths would contribute very little to the accuracy of the determination[6] of γ. If, however, we should enquire about the determination of α on the hypothesis that γ was known (or not correlated with α) we should have

$$\frac{1}{\sigma_\alpha^2} = -\frac{\partial^2 L}{\partial \alpha^2} = \frac{4n}{\alpha^2} \Sigma P_i Q_i [\tanh^{-1}(2P_i - 1)]^2 .$$

and it is clear that values near $P_i = 1/2$ will contribute very little. As a matter of fact those values of P in the neighborhood of 0.08 or 0.92 have the greatest weight. It is thus indicated that if we are assaying a biological to determine L.D.50 and we may assume from previous experience that the homogeniety, α, is known, we should aim to use such dilutions as will bring most of the observations near $P = 1/2$, but that if we are working with α unknown it is necessary to have a sufficient spread of P from the different dilutions so that α may be adequately determined.[7]

As $A = 2P_1 + 2P_2 + 2P_3 - 3$ and $B = P_3 - P_1$ are the combinations of the P's which enter into the determination of the parameters α, γ of the curve, the same curve will be obtained for any set of P's which give the same values of A and B, and in particular the values of P_1, P_2, P_3 on the fitted curve will be connected by the same relations. Hence in comparing the observed values with the fitted values we shall have

$$P_{1\,\text{obs}} - P_{1\,\text{fitted}} = P_{3\,\text{obs}} - P_{3\,\text{fitted}} = -1/2(P_{2\,\text{obs}} - P_{2\,\text{fitted}}).$$

In view of these relations we may easily set up all the different sets of s_i and $n - s_i$ which will lead to the same values of α and γ. For example if $s_1 = 8$, $s_2 = 15$, $s_3 = 20$ we have the three possibilities

s	8	15	20	7	17	19	6	19	18
$n - s$	12	5	0	13	3	1	14	1	2

The fitted values of s are 7.39, 16.23, 19.39. Any one of these tables may be compared with the fitted solution by a χ^2-test, but the test is not very good because of the small numbers in some of the six cells. If we are safe in using the general rule we have proposed for a cellular universe,[8] we should write as the relative probabilities of the three possibilities

$$\frac{1}{8\,!\,15\,!\,20\,!\,12\,!\,5\,!\,0'} \quad \frac{1}{7\,!\,17\,!\,19\,!\,13\,!\,3\,!\,1!'} \quad \frac{1}{6\,!\,19\,!\,18\,!\,14\,!\,1\,!\,2\,!}$$

which are as 663, 600, 50 with a sum of 1313 and give actual relative probabilities of 0.505, 0.457, 0.038, which would mean that the third set of values would be a bad fit judged at the 0.05 level of significance.[9] Actually with the variability of experimental animals one could hardly expect that the variation in different experiments should not exceed that due to pure chance.

[1] See these PROCEEDINGS, **29**, 79–85 (1943).

[2] Fisher, R. A., *Phil. Trans. Roy Soc.* (*London*), **A222**, 309–368 (1932). In this paper Fisher applies the method (p. 363) to another type of dilution series. Tables for the case of three series at tenth dilutions with $n = 10$ for each are given by Halvorson and Ziegler in their *Quantitative Bacteriology*, Burgess Publishing Co., Minneapolis, 1938. R. D. Gordon, these PROCEEDINGS, **24**, 212–215 (1938) has indicated that the results of Halvorson and Ziegler are not in accord with careful experimental findings and has suggested the replacement of Fisher's method of maximum likelihood by the older method of inverse probability, and has given a longer treatment in *Biometrika*, **31**, 167–180 (1939) followed by a comment by E. Pearson. If elaborate investigation shows that the principle of maximum likelihood applied to a certain hypothetical formulation of the problem of determining polution by dilution experiments does not give the right results, either the principle or the hypothetical formulation will have to be given up or modified; but for our present problem we shall accept the principle.

[3] Since $\alpha(x - \gamma) = \tanh^{-1} X$, $\alpha = \frac{1}{c}\tanh^{-1} C$, and $C = \frac{2B}{X^2 - AX + 2}$ from (9).

[4] These formulas will give the standard errors for any number of dilutions provided the summations are carried over all the dilutions and the curve has been fitted well enough by any manner so that P_i can be adequately determined from it. For the problem solved above in the text the values of the standard errors may be determined as follows: measuring x from the middle dilution as 0, $x_1 = -0.6931$, $x_3 = +0.6931$, $x_1 - \gamma = 0.1860$, $x_2 - \gamma = 0.5071$, $x_3 - \gamma = 1.2002$. On the fitted curve $4P_1Q_1 = \mathrm{sech}^2\,\alpha(x_1 - \gamma) = \mathrm{sech}^2\,(-0.2675) = 1 - \tanh^2\,(-0.2675) = 1 - (0.2612)^2 = 0.9318$. Similarly $4P_2Q_2 = 0.6124$, $4P_3Q_3 = 0.1190$. $\partial^2L/\partial\gamma^2 = -1.6632n\alpha^2$, $\partial^2L/\partial\alpha^2 = -0.3611n$, $\partial^2L/\partial\alpha\partial\gamma = 0.2800n\alpha$. Then $H = 0.5222n^2\alpha^2$, $\sigma_\alpha^2 = 3.185/n$ and for $n = 20$, $\sigma_\alpha^2 = 0.1592$, $\sigma_\gamma^2 = 0.6915/(n\alpha^2) = 0.3344/n = 0.01672$. We may therefore write $\gamma = -0.5071 \pm 0.1293$, $\alpha = 1.438 \pm 0.399$. If we should have a second sample of three dilutions with $P_1' = 0.05$, $P_2' = 0.30$, $P_3' = 0.75$ we should find $\gamma' = 0.3054 \pm 0.1190$, $\alpha' = 1.440 \pm 0.3652$. It is clear that $\alpha = \alpha'$ much more nearly than could be expected by sampling. The difference $\gamma' - \gamma = 0.8124 \pm 0.1757$, and the difference is therefore highly significant. The antilogarithm of 0.8124 is 2.25 and of 0.1757 = 1.19 which means that the ratio 2.25 of the strength of the first to that of the second is affected by a sampling factor of 1.19 or 0.84 which amounts to about $17^1/_2\%$ or $2.25 \pm$

0.39. It may be noted that the 3-dilution problem here worked out corresponds to the 2-dilution problem of our previous note (with P and P' interchanged) where the result was 2.24 ± 0.49. In this case the result of taking the two best P's (not two corresponding P's) from a set of three in each of two dilutions is not materially different from or much more poorly determined than the result coming from the somewhat more elaborate calculations using all three dilutions.

[5] For the cases of the previous footnote $r = 0.361$, $r' = -0.201$; in both of which the value of r^2 is small.

[6] Thus, in the illustration, $P_1 = 0.40$, $P_2 = 0.75$, $P_3 = 1.00$ as observed led to $P_1 = 0.37$, $P_2 = 0.81$, $P_3 = 0.97$ for the curve and these contributed respectively $4P_1Q_1 = 0.9318$, $4P_2Q_2 = 0.6124$, $4P_3Q_3 = 0.1190$ to $1/\sigma_\gamma^2$; if we had had an additional dilution giving a value $s_0 = 1$ or 2 and let us say $P_0 = 0.07$ on the average, its contribution would be 0.2604, which would be more than that due to $s_3 = 20$, and so far as the determination of γ goes it would have been better to use this dilution than the one which led to $s_3 = 20$; but in respect to the determination of γ' for which the first observed point was $s_1' = 1$, the weaker dilution would add $s_0' = 0$ and P_0' on the curve would be about 0.0076 giving a value of $4P_0'Q_0' = 0.030$ which would add practically nothing to the determination. When two biologicals are of strengths as different as these two it might be well to use different sets of three dilutions in comparing them.

[7] If we wished to determine only the difference between two values of L.D.50 in two biologicals with no desire to determine γ, γ', α or α' we could set up the maximum likelihood solution for $d = \gamma' - \gamma$, using $\gamma_0 = {}^1/_2(\gamma + \gamma')$, d, α and α' as four variables. This would come back to the solution obtained by treating α, γ together and α', γ' together and forming the difference $\gamma - \gamma'$ and its standard error. But if it were justifiable to assume that α, though unknown, were the same for both biologicals and only γ and γ' were different, we could set up the problem in terms of the three variables γ_0, α, d. The solution would still be the same as for $\gamma - \gamma'$ provided the values of P_i and P_i' were such as to give no correlations between α and γ or α and γ' in the separate solutions and if the correlations were small the solution would not differ very much either for the difference itself or for its standard error; α would be better determined, but that would be of slight advantage.

[8] These PROCEEDINGS, **28**, 378–384, 384–390 (1942), with especial reference to pages 382 and 388.

[9] The corresponding value of χ^2 is 6.2, indicating a probability level, with one degree of freedom, of 0.013 instead of 0.038. It may be noted that the mean values of any s is not the fitted value—thus, the mean value of s_1 is 7.47 instead of 7.39.

CONCERNING THE RELATION BETWEEN STRUCTURE AND ACTION OF XANTHONES ON DEHYDROGENATIONS BY FUSARIA*

BY LOUIS J. SCIARINI, ROBERT P. MULL, JOHN C. WIRTH AND F. F. NORD

DEPARTMENT OF ORGANIC CHEMISTRY, FORDHAM UNIVERSITY

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According to Schöpf,[1] the formation of natural substances in the living cell may be of three types. (*a*) The cell may have an enzymatic system designed for the highly specific synthesis of a certain substance. (*b*) The second type is the result of processes of general application performed by enzymes, e.g., hydrogenations, dehydrogenations, decarboxylation, etc. (*c*) Such cases as take place without the action of enzymes and are characterized by the formation in the growth of the cell of reactive organic substances, which upon contact in the cell yield isolable products, which are, in fact, chance products or intermediates in the synthesis of the former, when their further conversion within the cell proceeds slower than their synthesis.

In the course of enzyme studies[2] conducted at this laboratory with different fusaria, an attempt was made to approach the problem of the function of certain "waste materials," such as pigments in plant cells or in microörganisms. In an earlier investigation[3] the observation was made that *Fusarium oxysporum* contains a pigment, which may be related to aurofusarin.[4] Attempts to extract or to accumulate this pigment proved to be futile. Consequently, recourse was taken to *Fusarium graminearum* Schwabe (Fgra) which, when cultivated on certain media, develops with abundant deposition of a reddish orange pigment (rubrofusarin).

Recently it was observed[5] that the addition of nicotinic acid (NA) makes it possible more readily to synthesize dehydrogenating enzymes abundantly present in fusaria. It seemed justifiable to investigate whether there exists a functional relation between the two structurally different groups of substances.

Enzyme Material Used.—Fusarium lini Bolley (FlB) No. 5140 from the Biologische Reichsanstalt, Berlin-Dahlem, through the courtesy of Dr. H. Wollenweber. Fgra No. A 36-1-VIII from the University of Minnesota, through the courtesy of Dr. C. J. Eide. Stock cultures of the species were maintained on the following nutrient medium:

20.00 g. glucose
1.00 g. potassium nitrate
1.50 g. potassium phosphate (primary)
0.75 g. magnesium sulfate, $7H_2O$
1000 ml. water

and transferred at two-weeks intervals. The cultures were periodically examined to check their purity.

Cultural Conditions.—For the experiments with NA and the various xanthones, a salt solution consisting of the following:

5.00 g. potassium nitrate
5.00 g. potassium phosphate (primary)
0.75 g. magnesium sulfate, $7H_2O$
1000 ml. water

was sterilized at 120°C. under 15 pounds' pressure for 15 minutes.

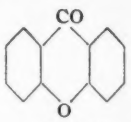
The isopropyl alcohol (Propol) was purified and the 81–81.7°C. fraction utilized as substrate, being added with sterile technique to the sterilized salt solution. In the case of NA, a previously sterilized water solution containing the required amount was added to the salt solution with sterile technique. With the various xanthones, the compound being investigated was first dissolved in Propol and then added to the salt solution. The concentration of Propol in all cases was approximately 0.4% and the initial pH 4.4. In all these experiments the FlB was grown in 125-ml. Erlenmeyer flasks containing 50 ml. of nutrient medium. Forty flasks were used for each series of experiments. Inoculation was by means of spores grown on the stock nutrient medium containing 2% agar.

For the production of the pigment a Raulin-Thom nutrient medium was used. A sterilincubator containing 14 Pyrex trays, each filled with 3 liters of nutrient medium, was used for the growth. The calculated amount of sterile 2 *N* sodium hydroxide was added later to change the pH to 8. Inoculations were by means of Fgra spores grown on the stock nutrient medium, containing 2% agar. After 3 weeks, the mats were removed, filtered, washed with water and dried in a vacuum oven at 40°C. The mats were then ground and exhaustively extracted† in a Soxhlet with petrol ether 40–60°C. Crude rubrofusarin separated upon cooling. This organism supplied us with 500 mg. of a crude composite pigment, obtained from 375 g. of dry mats. Purification was by means of sublimation and recrystallization. Chromatographic adsorption was also used as an alternative method for obtaining pure rubrofusarin, the analysis of which indicated that the pigment was a xanthone derivative, $C_{15}H_{12}O_5$ (see later).

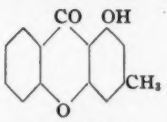
Analytical Methods.—Four flasks were removed for each analysis and the combined filtrates analyzed in duplicate. The nutrient medium was filtered from the mycelium and 100 ml. of the filtrate was made alkaline with 10 ml. of 1 *N* sodium hydroxide and distilled in an all-glass apparatus. About 85 ml. of the distillate was collected and the volume brought up to 100 ml. Twenty-ml. aliquots of the distillate were used for determining Propol and acetone. Propol was analyzed by addition of the aliquot to a

mixture of 10 ml. of 0.4 *N* potassium dichromate and 15 ml. of concentrated sulfuric acid at room temperature. This was let stand 30 minutes and diluted with water to 400 ml. Fifteen ml. of 20% potassium iodide solution were then added and titrated with 0.1 *N* sodium thiosulfate to the starch end-point. Acetone determinations[6] were carried out as heretofore. Mycelial weights were determined after 13 days by filtering, drying and weighing[5] the mycelium from 5 flasks.

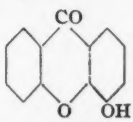
Discussion.—Starting with a Propol solution of the pigment, the effect of solutions upon the rate of dehydrogenation by FlB of the following substituted and basic xanthones was investigated:



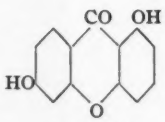
Xanthone



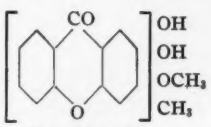
1-OH, 3-CH_3 Xanthone



4-OH Xanthone



1,6-diOH Xanthone



Rubrofusarin

The table presented below shows the extent of effect observed on the rate of dehydrogenation of Propol and accumulation of acetone in the presence of given amounts of these compounds as compared with the magnitude of the rate of the same reaction effected by adding NA. Mat weight determinations at the end of each series of experiments complement the observations.

It can be seen, that in accordance with the structural formulae of our xanthones, the following relations exist: xanthone (e.g., 8th day: 12.84%) and NA (in accordance with the concentrations: 1.99%, 2.69%, 4.13%, 5.69%) increase measurably the rate of dehydrogenation as compared with the blank. The three intermediates tend to show, in general, an increase (e.g., 8th day: 11.34%, 10.66%, 5.33%) in this rate to a distinctly lesser extent, and the natural pigment definitely retards the progress of dehydrogenation (e.g., 8th day: −3.01%) in accordance with the increasing number of hydroxyl groups and complexity of the xanthone molecule.

In evaluating the analytical data it has to be borne in mind that two dehydrogenations proceed parallel to one another. The dehydrogenation of the Propol is attended by that of the acetone formed. The latter reaction leads[6] to formaldehyde via methanol as intermediary:

$$CH_3COCH_3 + H_2O \rightarrow CH_3CHO + CH_3OH$$
$$CH_3OH—H_2 \rightarrow HCOH$$

TABLE 1

DEHYDROGENATION OF ISOPROPYL ALCOHOL*

Concentrations of various xanthones and nicotinic acid are expressed in γ per 1000 ml.

	BLANK		XANTHONE 1000		1-OH 3-CH_3 XANTHONE 1000		4-OH XANTHONE 1000		1,6-diOH XANTHONE 1000		RUBRO-FUSARIN 1000		BLANK		NA 500		NA 1000		NA 5000		NA 10,000	
DAY	PRO-POL	ACE-TONE	PRO-POL	ACE-TONE	PRO-POL	ACE-TONE	PRO-POL	ACE-TONE	PRO-POL	ACE-TONE	PRO-POL	ACE-TONE	PRO-POL	ACE-TONE	PRO-POL	ACE-TONE	PRO-POL	ACE-TONE	PRO-POL	ACE-TONE	PRO-POL	ACETONE
0	180.0		181.6		182.7		186.0		183.0		180.0		183.5		187.5		187.0		189.0		185.0	
7	63.0	14.7	72.1	15.2	72.2	15.2	68.0	17.0	65.4	12.0	60.3	12.2	69.5	14.5	72.3	11.7	72.8	13.7	72.5	12.6	74.0	14.0
8	73.2		82.6		81.5		81.0		77.1		71.0		80.5		79.0		80.5		80.5		81.4	
9	86.3	17.3	91.6	19.3	90.6	21.0	94.1	18.7	88.9	17.2	80.3	14.2	88.8	16.8	89.0	15.8	85.0	16.0	93.2	17.3	90.7	15.3
10	106.0		110.3		112.2		110.0		104.3		96.3		101.7		103.3		104.1		98.5		104.3	
11	108.8	22.7	111.1	24.5	119.2	26.7	124.0	32.2	119.3	28.5	100.3	19.8	108.0	20.2	112.5	20.0	114.7	20.5	120.1	22.5	120.4	25.0
12	120.8		122.9		123.2		130.5		129.7		116.7		121.2		123.0		127.5		129.0		132.0	
13	131.8	33.8	139.8	32.6	138.2	29.0	134.3	35.5	144.0	28.1	126.8	32.9	130.5	25.8	133.5	24.3	135.8	28.0	137.2	28.5	139.8	26.3
MYCELIUM WEIGHT ON 13TH DAY																						
	26 mg.		29.4 mg.		35.0 mg.		39.9 mg.		41.7 mg.		35.5 mg.		31.7 mg.		29.3 mg.		35.4 mg.		32.4 mg.		42.5 mg.	

* Measured as amount in mgs. disappearing per 50 ml. of nutrient medium.

The extremely high rate of this reaction is recognizable towards the end and, consequently, the terminal Propol values appear to be higher in the case of extended experiments.

Although the increase in mat weight in the case of basic xanthone is only slight, the influence on the rate of dehydrogenation was greatest. In the case of the pigment, however, an approximately 40% increase of the final mat weight still was accompanied by a definite retardation of the rate of dehydrogenation.

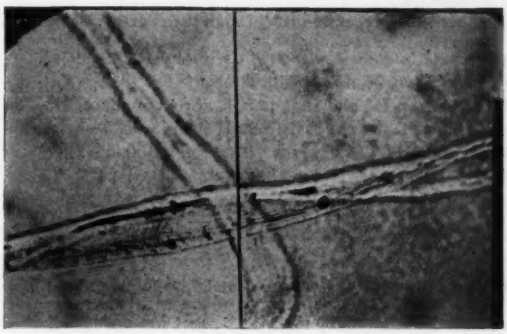


FIGURE 1
F1B grown on a Propol solution of xanthone (9th day, × 400).

FIGURE 2
F1B grown on a Propol solution of rubrofusarin (9th day, × 400).

Contrary to figure 1 above, the fungus in figure 2‡ indicates a visible deposition of the pigment excreted by Fgra, which is not utilized by F1B. This deposition is accompanied by enhanced growth.

These experiments seem to represent the first attempt to explain a possible mode of functioning of "waste products" in microörganisms.

Summary.—From the recorded values it is evident that the xanthones applied both augment and decrease the growth of FlB, accordingly giving rise to a higher or retarded rate of dehydrogenation of Propol, as compared with the values of the blank or with the effect of NA.

* This work was supported in part by a grant from the Rockefeller Foundation.

† About 100 g. of a mixture of fats were collected in the course of extraction which are being further investigated.

‡ The microphotographs were obtained through the courtesy of Dr. L. Yanowski.

[1] Schöpf, C., *Proc. 9th Internat. Congress of Chemistry*, **5**, 189 (1934).

[2] Nord, F. F., *Chem. Rev.*, **26**, 452 (1940).

[3] Nord, F. F., Hofstetter, H., and Damman, E., *Biochem. Zeit.*, **293**, 235 (1937).

[4] Ashley, J. N., Hobbs, B. C., and Raistrick, H., *Biochem. Jour.*, **31**, 385 (1937).

[5] Wirth, John C., and Nord, F. F., *Arch. Biochem.*, **1**, 150 (1942).

[6] Goepfert, G. J., *Jour. Biolog. Chem.*, **140**, 530 (1941).

NOTICE. Owing to the preoccupation of members of the NATIONAL ACADEMY OF SCIENCES and of the NATIONAL RESEARCH COUNCIL with scientific aspects of the war effort, the manuscripts available for the March issue were so few that they were held over for this combined March-April number. It is not unlikely that from time to time similar combinations of numbers may be advisable, and it may not be possible always to give advance notice thereof.